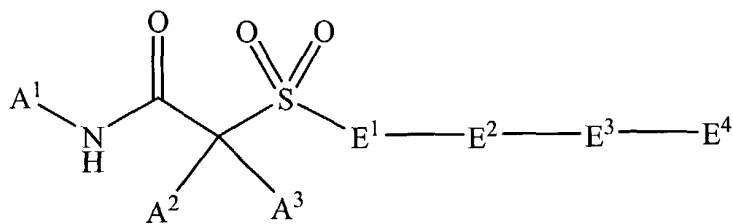


WE CLAIM:

1. A compound or a salt thereof, wherein:  
the compound corresponds in structure to Formula (1-1):



(1-1); and

A<sup>1</sup> is selected from the group consisting of hydrogen, hydroxy, carbocycloxy, and heterocycloxy; and

as to A<sup>2</sup> and A<sup>3</sup>:

A<sup>2</sup> and A<sup>3</sup>, together with the carbon to which they are bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R<sup>x</sup> substituents, or

A<sup>2</sup> and A<sup>3</sup> are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocycloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3  
independently selected R<sup>x</sup> substituents, and

any member of such group optionally is substituted with two  
substituents such that the two substituents, together with the atom(s) to  
5 which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the heterocyclyl and carbocyclyl optionally are  
substituted with up to 3 independently selected R<sup>x</sup> substituents;  
and

E<sup>1</sup> is aryl optionally substituted with one or more independently selected R<sup>x</sup>  
10 substituents; and

E<sup>2</sup> is selected from the group consisting of aryl and heteroaryl, wherein:

the aryl or heteroaryl optionally substituted with one or more  
independently selected R<sup>x</sup> substituents; and

E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-,  
15 -N(R<sup>b</sup>)-, -C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-,  
-S-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-,  
-C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-, alkyl,  
alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is  
20 substituted with one or more independently selected R<sup>c</sup> substituents; and

E<sup>4</sup> is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxyalkyl,  
alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl,  
alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl,  
carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl,

25 wherein any such group:

comprises at least two carbon atoms, and

is substituted with one or more independently-selected halogen, and

is optionally substituted with one or more independently selected R<sup>d</sup>  
substituents; and

30 each R<sup>x</sup> is independently selected from the group consisting of halogen, cyano,  
hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,

R<sup>b</sup>-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy, R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocyclyoxy, carbocyclyoxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyoxy, heterocyclyoxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and -R<sup>x1</sup>-R<sup>x2</sup>, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently selected alkyl; and

each R<sup>x1</sup> is independently selected from the group consisting of -C(O)-, -C(S)-, -C(NR<sup>y</sup>)-, and -S(O)<sub>2</sub>-; and

each R<sup>y</sup> is independently selected from the group consisting of hydrogen and hydroxy; and

each R<sup>x2</sup> is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R<sup>b</sup>-oxyalkyl, alkenyloxy, alkynyloxy, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy, R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocyclyoxy, carbocyclyoxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyoxy, and heterocyclyoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

5                   the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R<sup>b</sup> is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocycloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

10

15

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

20

each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

25

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

30

each R<sup>d</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl,

-N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>g</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl, -O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclylalkyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>h</sup> is independently selected from the group consisting of hydrogen, alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

2. A compound or salt thereof according to claim 1, wherein E<sup>1</sup> is phenyl.

3. A compound or salt thereof according to claim 2, wherein A<sup>1</sup> is tetrahydropyranyl.

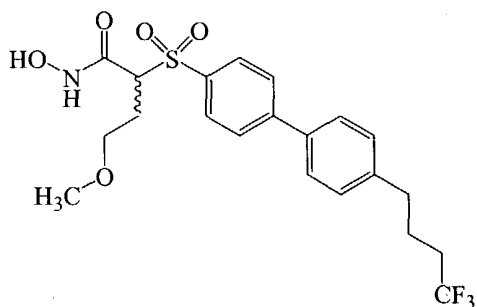
4. A compound or salt thereof according to claim 2, wherein A<sup>1</sup> is hydrogen.

5. A compound or salt thereof according to claim 2, wherein A<sup>1</sup> is hydroxy.

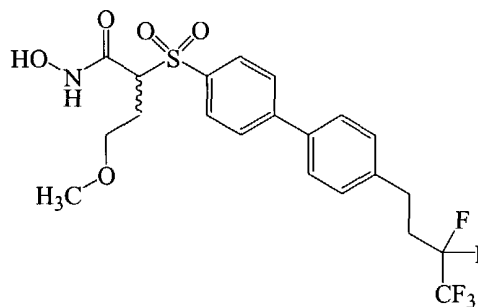
6. A compound or salt thereof according to claim 5, wherein A<sup>2</sup> is hydrogen.

5 7. A compound or salt thereof according to claim 6, wherein A<sup>3</sup> is alkoxyalkyl.

8. A compound or salt thereof according to claim 7, wherein the compound is selected from the group consisting of:

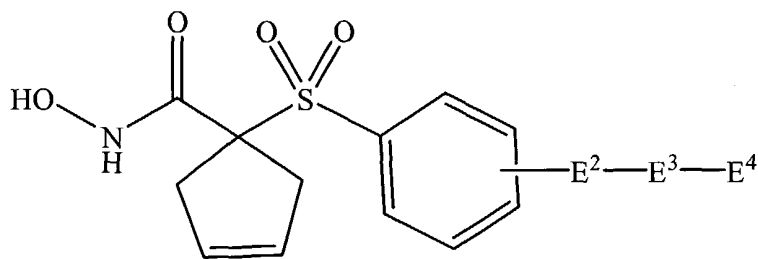


(8-1), and



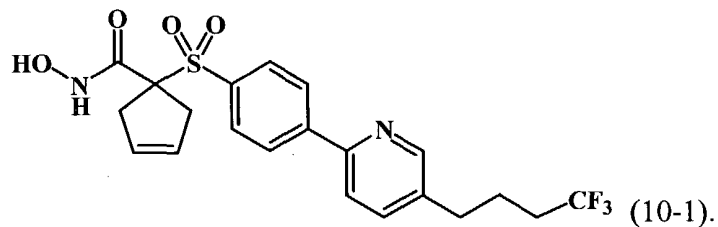
(8-2).

10 9. A compound or salt thereof according to claim 5, wherein the compound corresponds in structure to Formula (9-1):



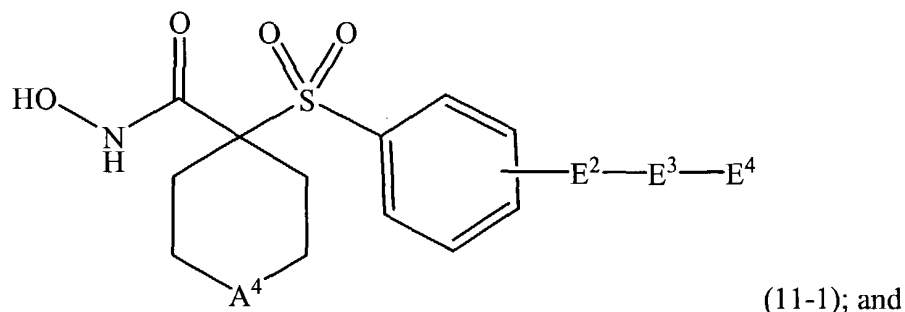
(9-1).

10. A compound or salt thereof according to claim 9, wherein the compound  
15 corresponds in structure to Formula (10-1):



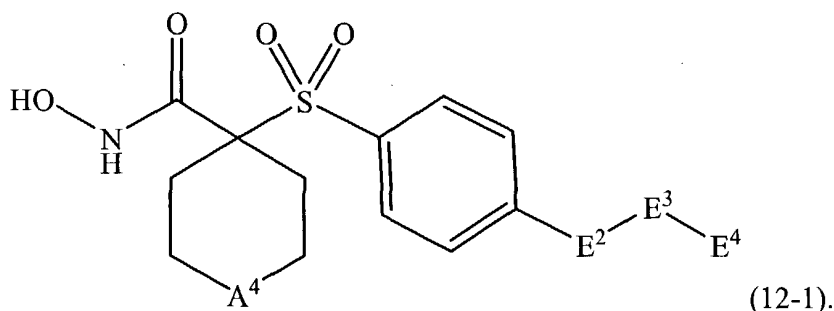
(10-1).

11. A compound or salt thereof according to claim 5, wherein:  
the compound corresponds in structure to Formula (11-1):

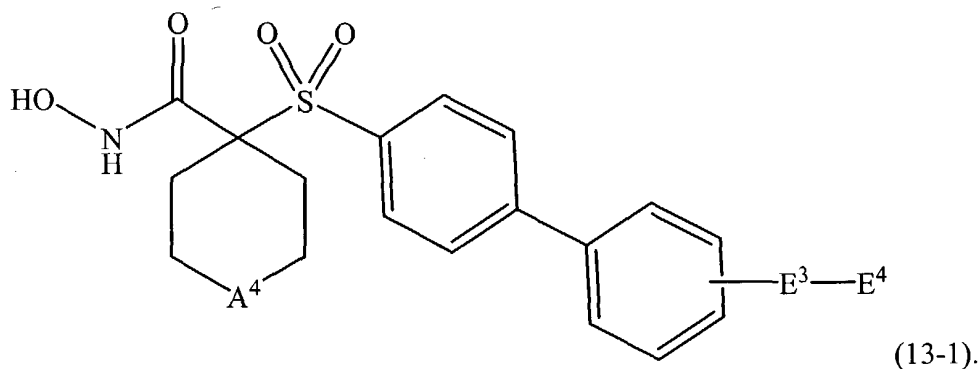


A<sup>4</sup> is selected from the group consisting of -O-, -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-.

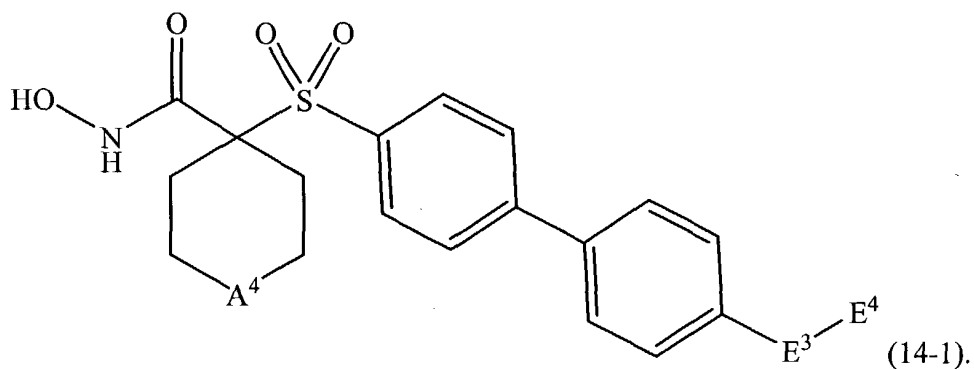
12. A compound or salt thereof according to claim 11, wherein the compound corresponds in structure to Formula (12-1):



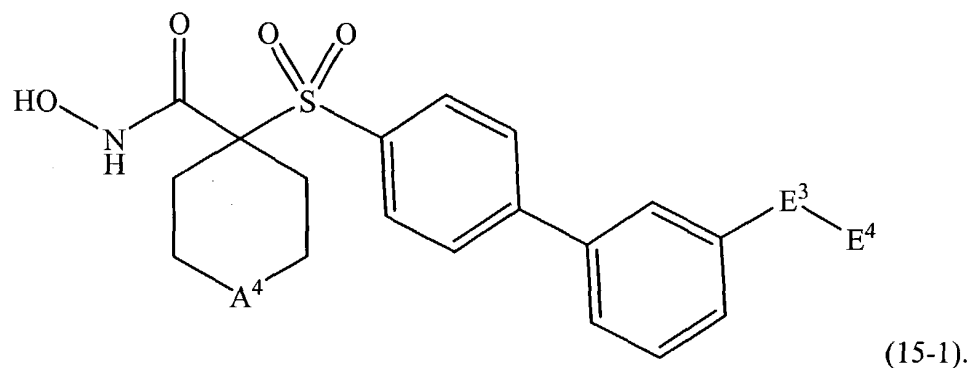
13. A compound or salt thereof according to claim 12, wherein the compound corresponds in structure to Formula (13-1):



14. A compound or salt thereof according to claim 13, wherein the compound corresponds in structure to Formula (14-1):

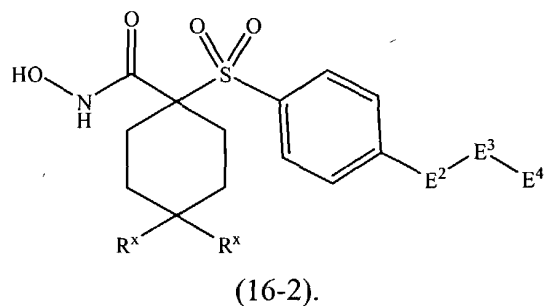
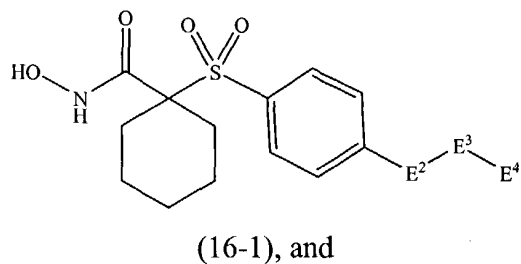


15. A compound or salt thereof according to claim 13, wherein the compound corresponds in structure to Formula (15-1):



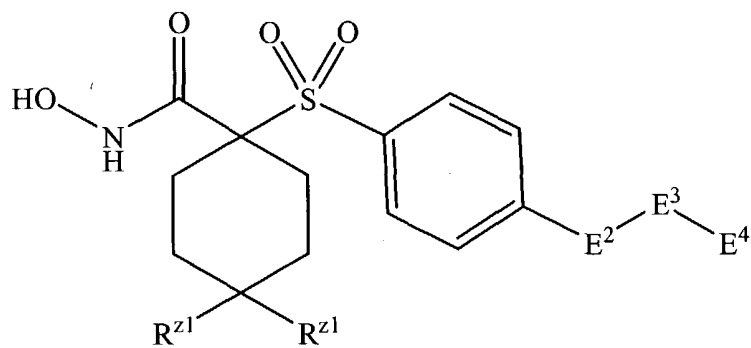
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16. A compound or salt thereof according to claim 12, wherein the compound corresponds in structure to a formula selected from the group consisting of:



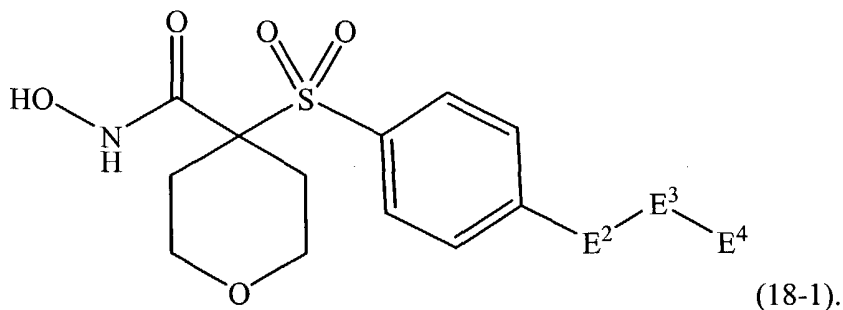
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17. A compound or salt thereof according to claim 16, wherein:  
the compound corresponds in structure to Formula (17-1):

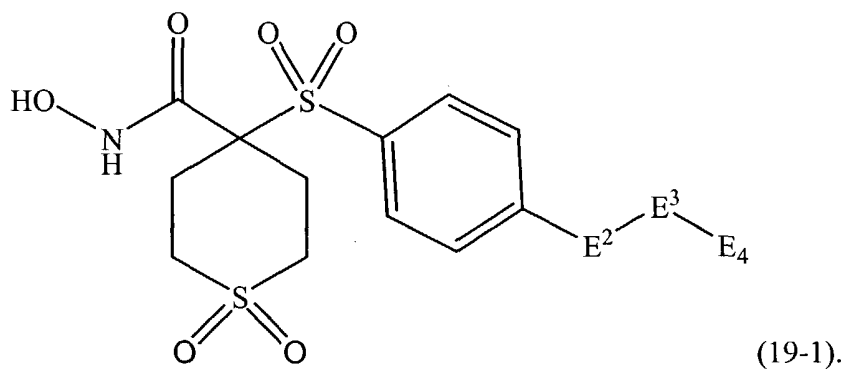


each  $R^{z1}$  is independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, and alkoxyalkoxy.

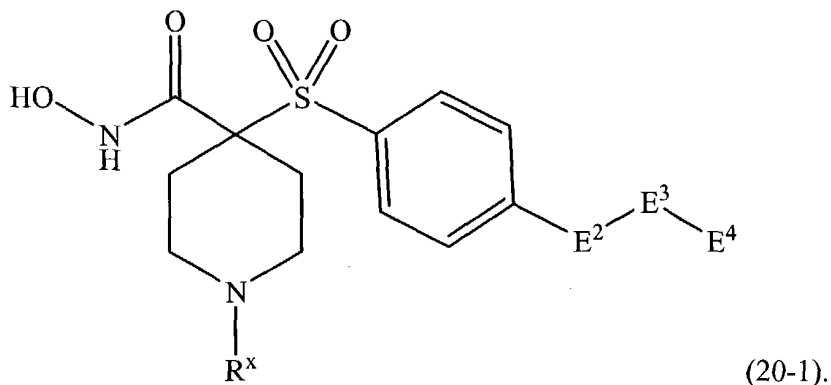
- 5        18. A compound or salt thereof according to claim 12, wherein the compound corresponds in structure to Formula (18-1):



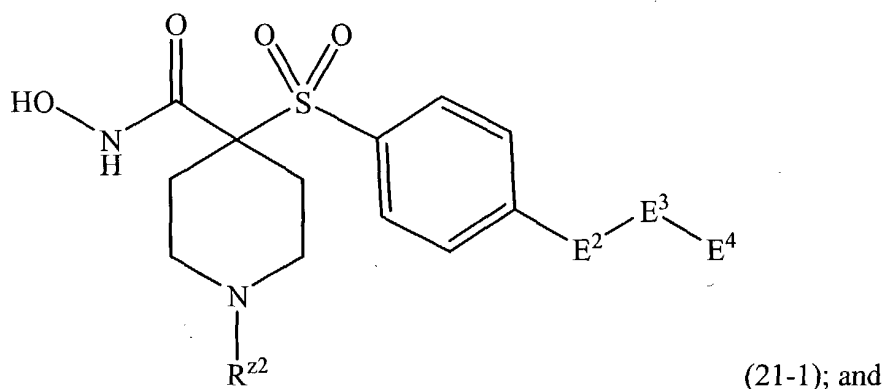
- 10       19. A compound or salt thereof according to claim 12, wherein the compound corresponds in structure to Formula (19-1):



20. A compound or salt thereof according to claim 12, wherein the compound corresponds in structure to Formula (20-1):



21. A compound or salt thereof according to claim 20, wherein:  
the compound corresponds in structure to Formula (21-1):



$R^{z2}$  is selected from the group consisting of alkyl, alkoxyalkyl, cycloalkyl, formyl, heterocycloalkylcarbonyl, and dialkylaminocarbonyl.

22. A compound or salt thereof according to claim 12, wherein  $E^2$  is phenyl substituted with one or more independently selected  $R^x$  substituents.

23. A compound or salt thereof according to claim 12, wherein  $E^2$  is phenyl.

24. A compound or salt thereof according to claim 12, wherein  $E^2$  is heteroaryl substituted with one or more independently selected  $R^x$  substituents.

25. A compound or salt thereof according to claim 12, wherein  $E^2$  is heteroaryl.

26. A compound or salt thereof according to claim 25, wherein E<sup>2</sup> is selected from the group consisting of furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiodiazolyl, oxadiazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, oxathiazinyl, oxepinyl, thiepinyl, benzofuranyl, isobenzofuranyl, benzoxazolyl, benzoisoxazolyl, benzothienyl, isobenzothienyl, benzothiazolyl, benzoisothiazolyl, benzothiadiazolyl, indolizinyl, pyranopyrrolyl, quinolinyl, isoquinolinyl, naphthyridinyl, phthalazinyl, quinoxalinyl, quinazolinyl, cinnolinyl, pteridinyl, and acridinyl.

27. A compound or salt thereof according to claim 26, wherein E<sup>2</sup> is a 5-member heteroaryl.

28. A compound or salt thereof according to claim 27, wherein E<sup>2</sup> is selected from the group consisting of thienyl and oxadiazolyl.

29. A compound or salt thereof according to claim 26, wherein E<sup>2</sup> is a 6-member heteroaryl.

30. A compound or salt thereof according to claim 29, wherein E<sup>2</sup> is selected from the group consisting of pyridinyl, pyrazinyl, and pyrimidinyl.

31. A compound or salt thereof according to claim 12, wherein E<sup>4</sup> is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein any such group:

comprises at least two carbon atoms, and

is substituted with one or more fluoro, and

is optionally substituted with one or more independently selected R<sup>d</sup>

substituents.

32. A compound or salt thereof according to claim 12, wherein E<sup>4</sup> is halo-C<sub>2</sub>-C<sub>6</sub>-alkyl.

33. A compound or salt thereof according to claim 32, wherein E<sup>4</sup> is C<sub>2</sub>-C<sub>6</sub>-alkyl substituted with one or more fluoro.

34. A compound or salt thereof according to claim 32, wherein E<sup>4</sup> is C<sub>2</sub>-C<sub>6</sub>-alkyl partially substituted with one or more independently selected halogen.

35. A compound or salt thereof according to claim 34, wherein E<sup>4</sup> is C<sub>1</sub>-C<sub>5</sub>-alkyl substituted with trifluoromethyl.

36. A compound or salt thereof according to claim 35, wherein E<sup>4</sup> is selected from the group consisting of -(CH<sub>2</sub>)<sub>2</sub>-CF<sub>3</sub> and -(CH<sub>2</sub>)<sub>3</sub>-CF<sub>3</sub>.

37. A compound or salt thereof according to claim 34, wherein E<sup>4</sup> is selected from the group consisting of:

-CF<sub>2</sub>-CH<sub>3</sub>, and

C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with -CF<sub>2</sub>-CH<sub>3</sub>.

38. A compound or salt thereof according to claim 37, wherein E<sup>4</sup> is selected from the group consisting of -CH<sub>2</sub>-CF<sub>2</sub>-CH<sub>3</sub> and -(CH<sub>2</sub>)<sub>2</sub>-CF<sub>2</sub>-CH<sub>3</sub>.

39. A compound or salt thereof according to claim 34, wherein E<sup>4</sup> is selected from the group consisting of:

-CF<sub>2</sub>-CF<sub>3</sub>, and

C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with -CF<sub>2</sub>-CF<sub>3</sub>.

40. A compound or salt thereof according to claim 39, wherein E<sup>4</sup> is selected from the group consisting of -CH<sub>2</sub>-CF<sub>2</sub>-CF<sub>3</sub> and -(CH<sub>2</sub>)<sub>2</sub>-CF<sub>2</sub>-CF<sub>3</sub>.

41. A compound or salt thereof according to claim 34, wherein E<sup>4</sup> is C<sub>2</sub>-C<sub>6</sub>-alkyl comprising a carbon atom bonded to at least one hydrogen and at least one halogen.

42. A compound or salt thereof according to claim 41, wherein E<sup>4</sup> is C<sub>2</sub>-C<sub>6</sub>-alkyl comprising a carbon atom bonded to at least one hydrogen and at least one fluoro.

43. A compound or salt thereof according to claim 42, wherein E<sup>4</sup> is C<sub>1</sub>-C<sub>5</sub>-alkyl substituted with -CF<sub>2</sub>H.

44. A compound or salt thereof according to claim 43, wherein E<sup>4</sup> is -(CH<sub>2</sub>)<sub>3</sub>-CF<sub>2</sub>H.

45. A compound or salt thereof according to claim 42, wherein E<sup>4</sup> is C<sub>1</sub>-C<sub>5</sub>-alkyl substituted with -CH<sub>2</sub>F.

46. A compound or salt thereof according to claim 45, wherein E<sup>4</sup> is -(CH<sub>2</sub>)<sub>3</sub>-CH<sub>2</sub>F.

47. A compound or salt thereof according to claim 42, wherein E<sup>4</sup> is selected from the group consisting of:  
-CF<sub>2</sub>-CF<sub>2</sub>H, and  
C<sub>1</sub>-C<sub>4</sub>-alkyl substituted with -CF<sub>2</sub>-CF<sub>2</sub>H

48. A compound or salt thereof according to claim 47, wherein E<sup>4</sup> is selected from the group consisting of -CF<sub>2</sub>-CF<sub>2</sub>H and -CH<sub>2</sub>-CF<sub>2</sub>-CF<sub>2</sub>H.

49. A compound or salt thereof according to claim 12, wherein E<sup>4</sup> is halo-C<sub>2</sub>-C<sub>4</sub>-alkyl.

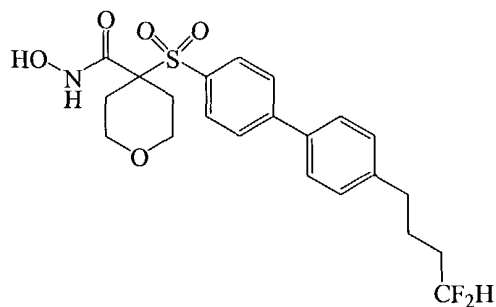
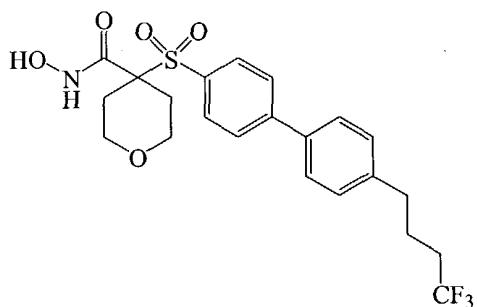
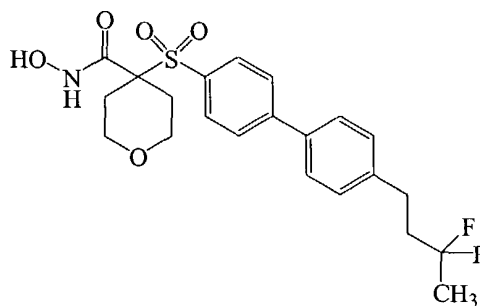
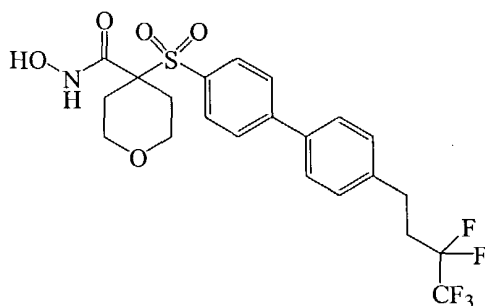
50. A compound or salt thereof according to claim 49, wherein E<sup>3</sup> is a bond.

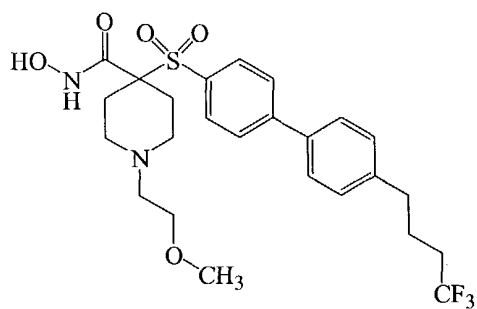
51. A compound or salt thereof according to claim 50, wherein E<sup>4</sup> is halo-C<sub>3</sub>-C<sub>4</sub>-alkyl.

52. A compound or salt thereof according to claim 51, wherein E<sup>4</sup> is selected  
5 from the group consisting of -(CH<sub>2</sub>)<sub>2</sub>-CF<sub>3</sub>, -(CH<sub>2</sub>)<sub>3</sub>-CH<sub>2</sub>F, -(CH<sub>2</sub>)<sub>3</sub>-CF<sub>2</sub>H, -(CH<sub>2</sub>)<sub>2</sub>-CF<sub>2</sub>-CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>3</sub>-CF<sub>3</sub>, -(CH<sub>2</sub>)<sub>2</sub>-CF<sub>2</sub>-CF<sub>3</sub>, and -(CH<sub>2</sub>)<sub>2</sub>-C(CF<sub>3</sub>)<sub>2</sub>F.

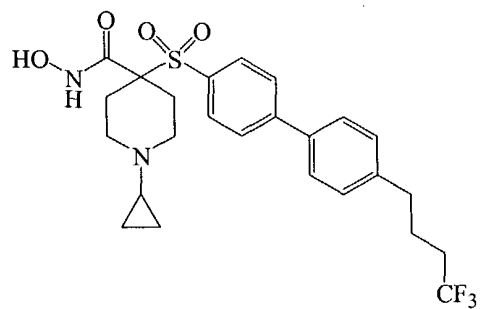
53. A compound or salt thereof according to claim 52, wherein E<sup>2</sup> is phenyl  
optionally substituted with one or more substituents independently selected from the  
10 group consisting of halogen and haloalkyl.

54. A compound or salt thereof according to claim 53, wherein the compound is  
selected from the group consisting of:

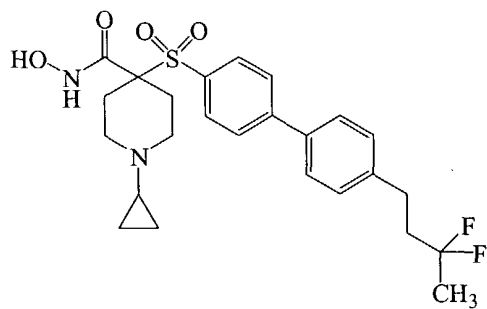




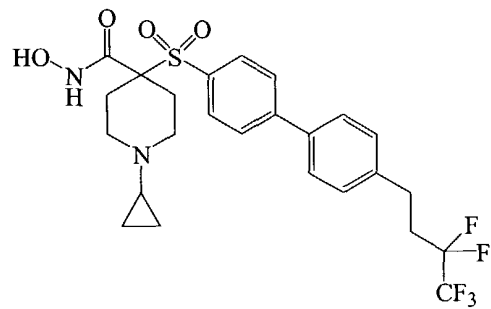
(54-5),



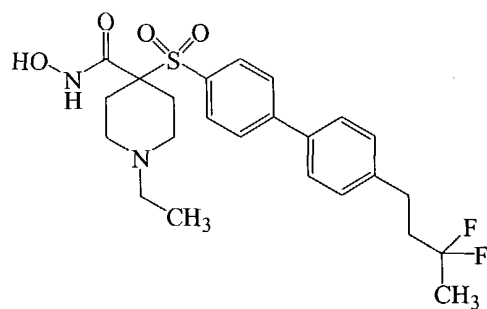
(54-6),



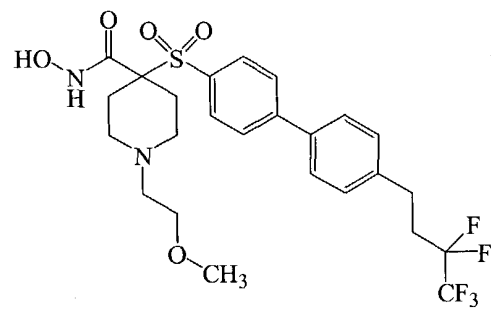
(54-7),



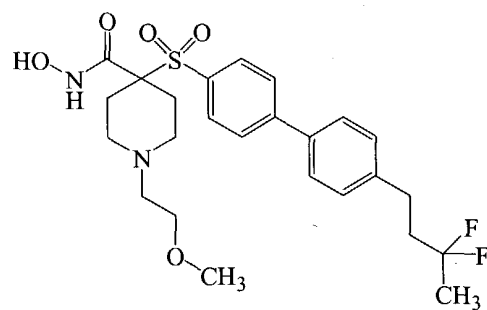
(54-8),



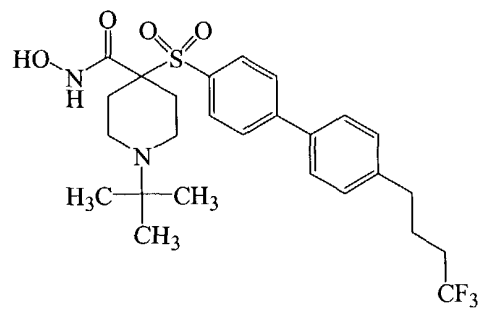
(54-9),



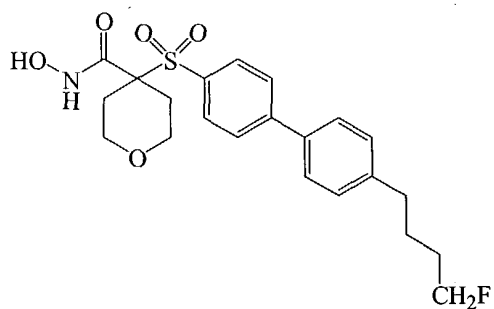
(54-10),



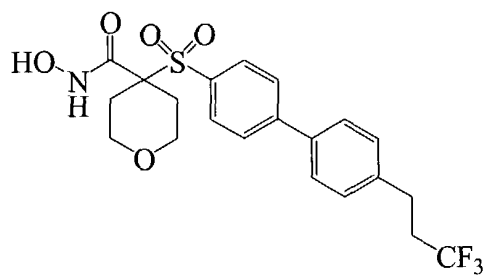
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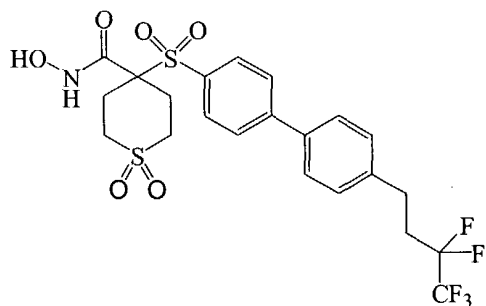
(54-12),



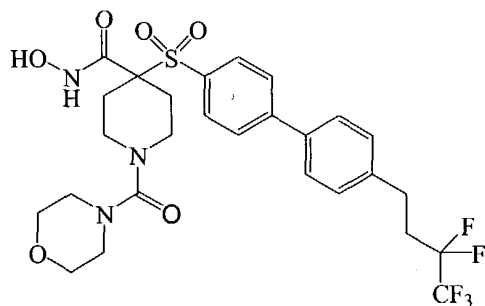
(54-13),



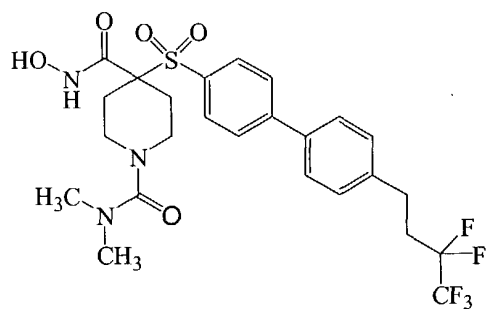
(54-14),



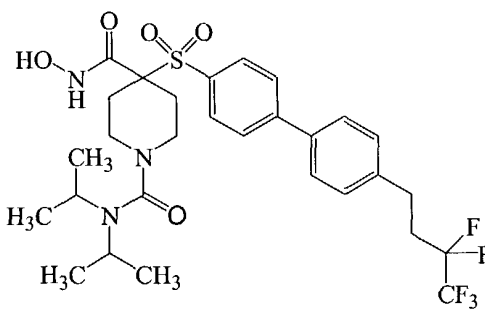
(54-15),



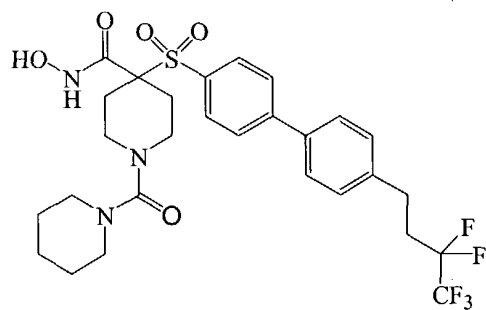
(54-16),



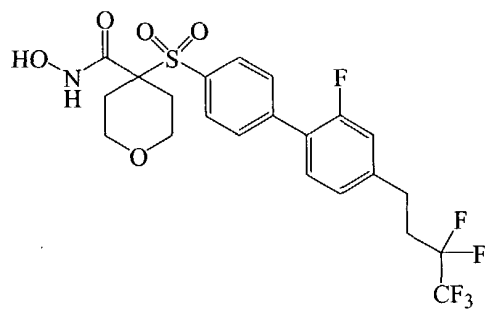
(54-17),



(54-18),



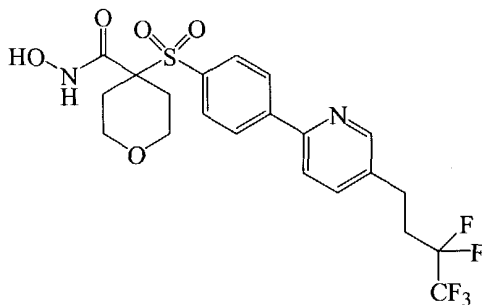
(54-19), and



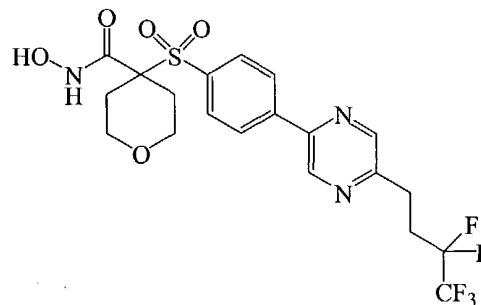
(54-20).

55. A compound or salt thereof according to claim 52, wherein E<sup>2</sup> is selected from the group consisting of pyridinyl, pyrazinyl, and pyrimidinyl.

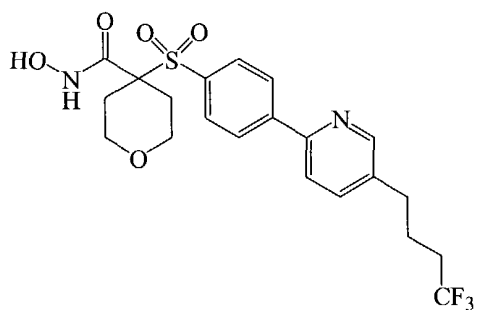
56. A compound or salt thereof according to claim 55, wherein the compound is selected from the group consisting of:



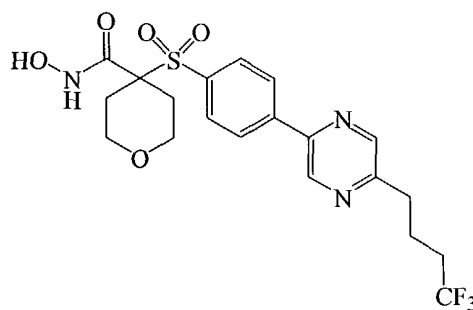
(56-1),



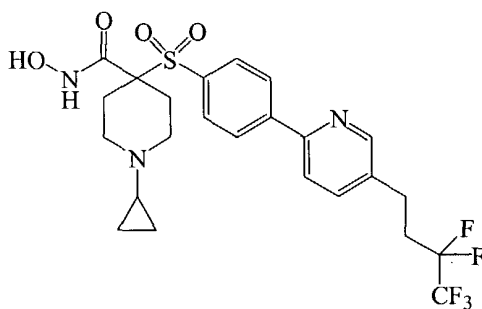
(56-2),



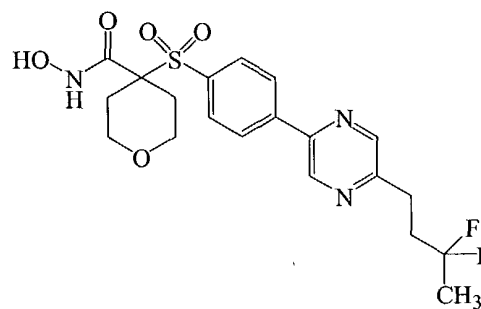
(56-3),



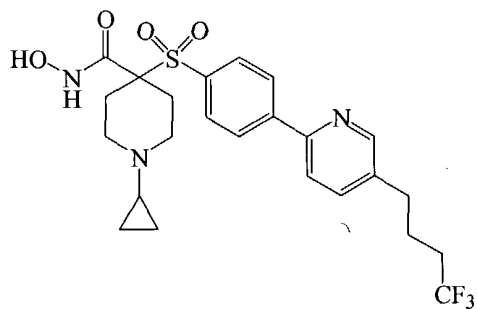
(56-4),



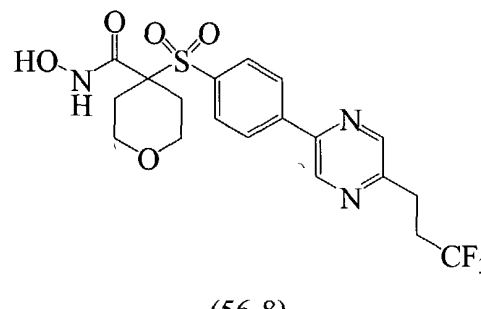
(56-5),



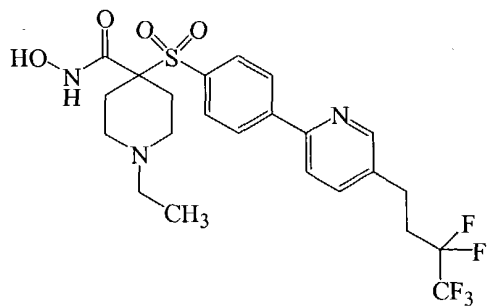
(56-6),



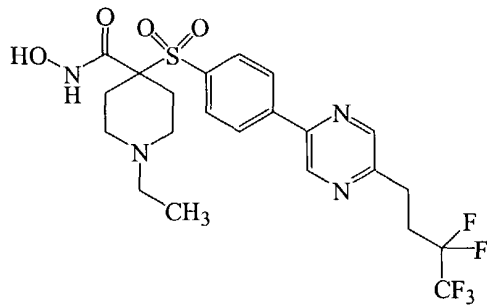
(56-7),



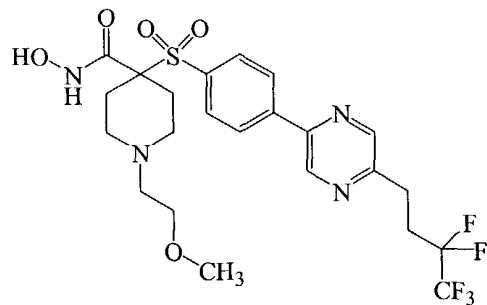
(56-8),



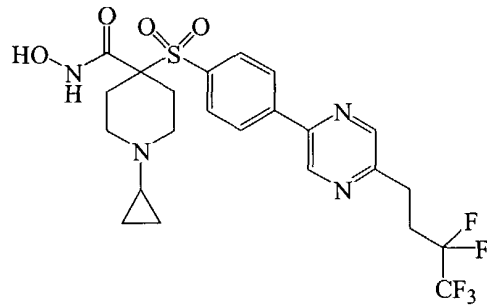
(56-9),



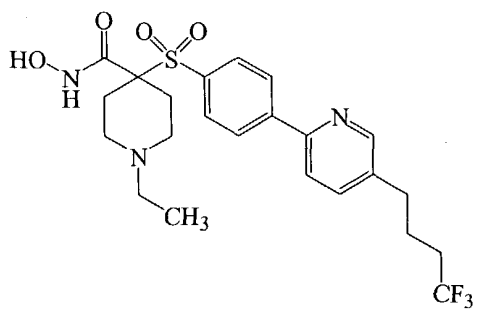
(56-10),



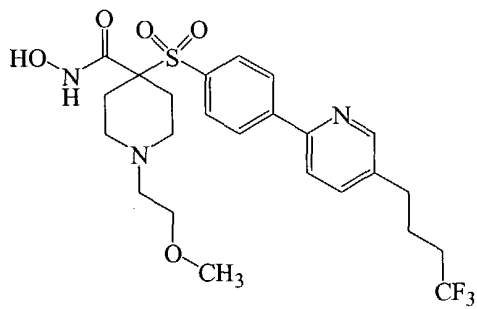
(56-11),



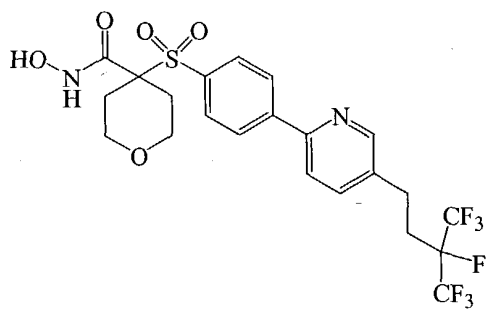
(56-12),



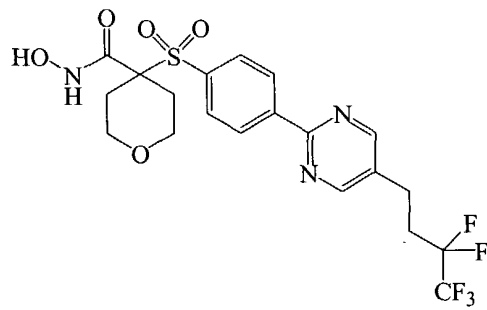
(56-13),



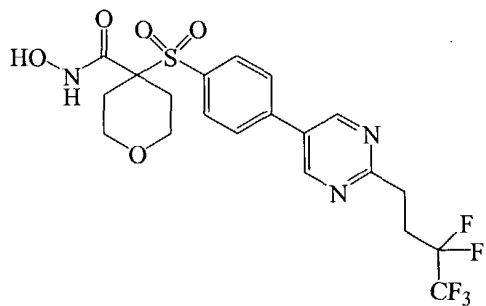
(56-14),



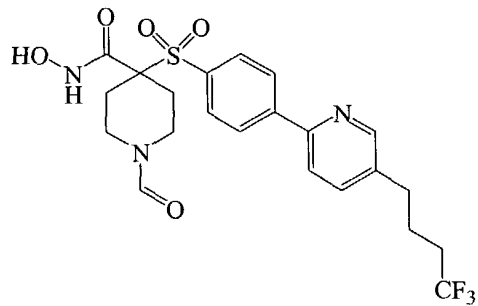
(56-15),



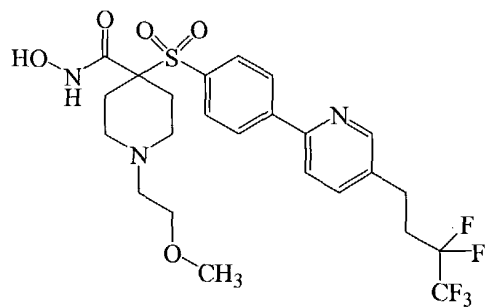
(56-16),



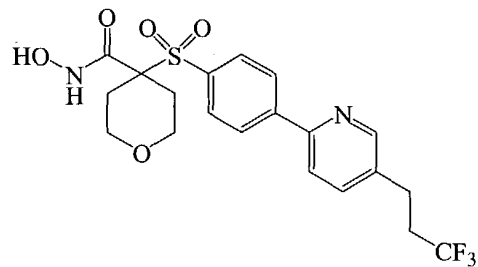
(56-17),



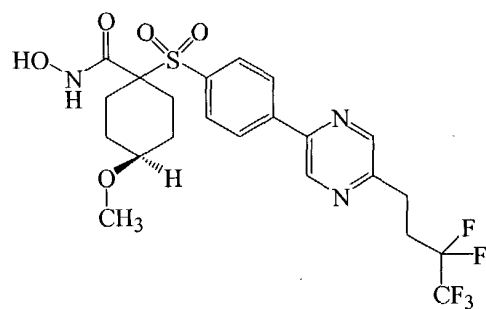
(56-18),



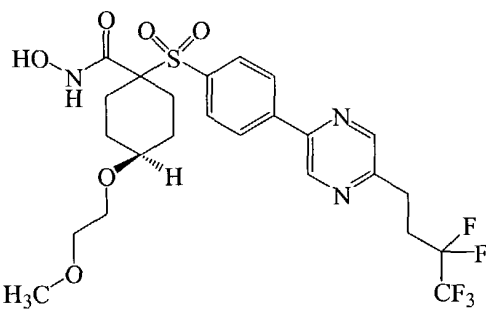
(56-19),



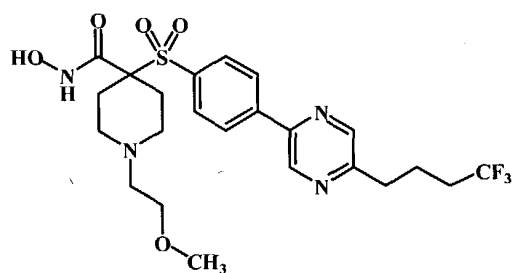
(56-20),



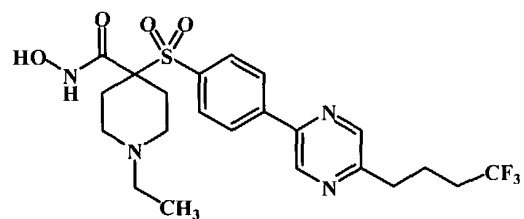
(56-21),



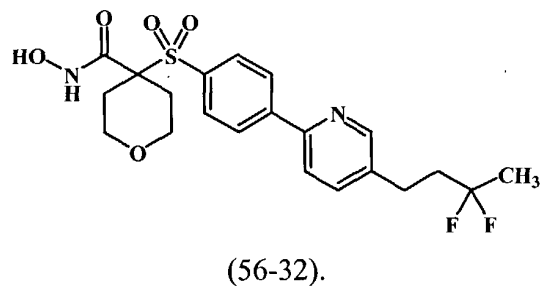
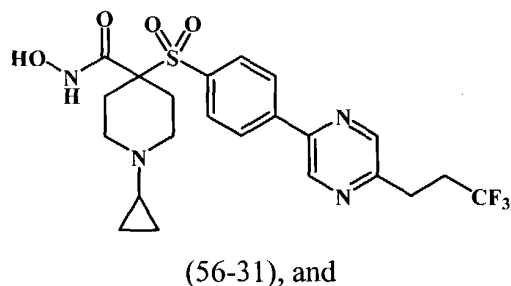
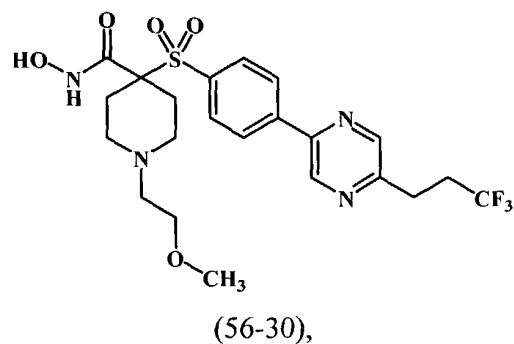
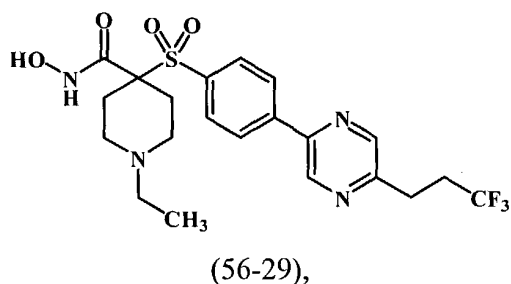
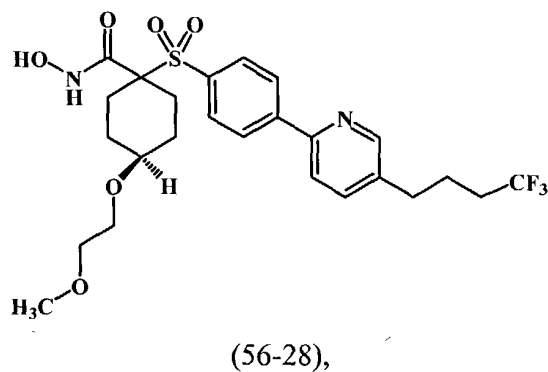
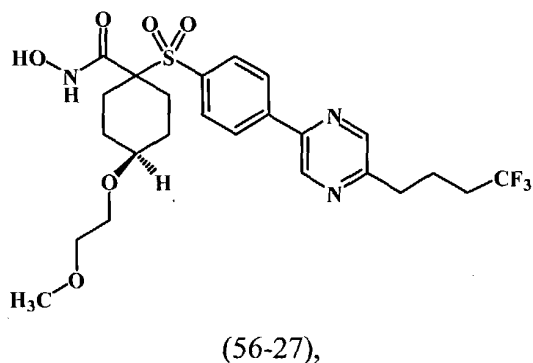
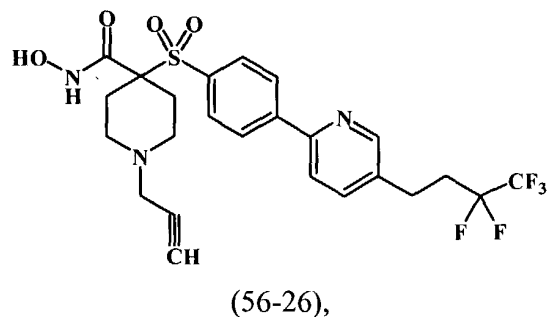
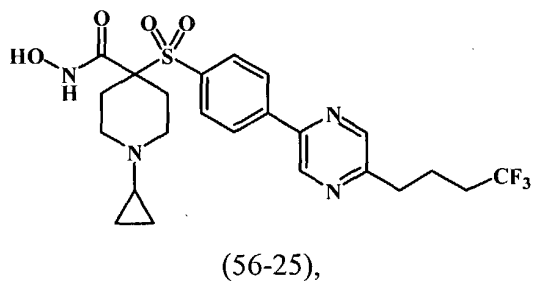
(56-22),



(56-23),



(56-24),

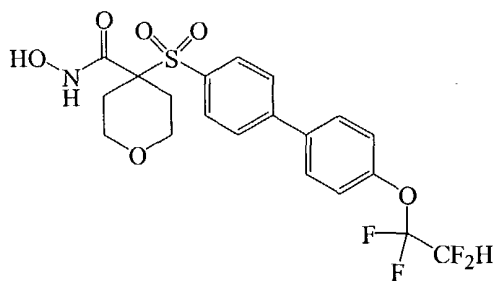


57. A compound or salt thereof according to claim 49, wherein E<sup>3</sup> is -O-.

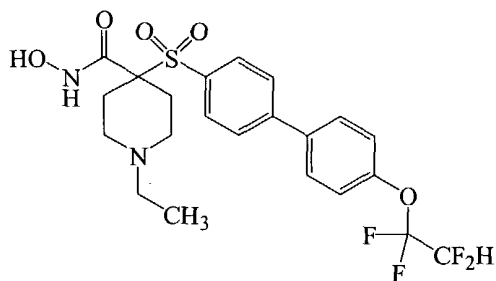
58. A compound or salt thereof according to claim 57, wherein E<sup>4</sup> is selected from the group consisting of -CF<sub>2</sub>-CF<sub>2</sub>H, -(CH<sub>2</sub>)<sub>3</sub>-CF<sub>3</sub>, -CH<sub>2</sub>-CF<sub>2</sub>-CH<sub>3</sub>, -CH<sub>2</sub>-CF<sub>2</sub>-CF<sub>2</sub>H, and -CH<sub>2</sub>-CF<sub>2</sub>-CF<sub>3</sub>.

59. A compound or salt thereof according to claim 58, wherein E<sup>2</sup> is phenyl.

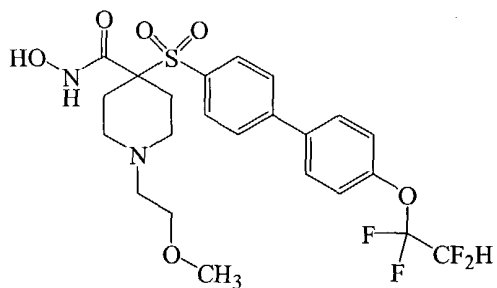
60. A compound or salt thereof according to claim 59, wherein the compound is  
5 selected from the group consisting of:



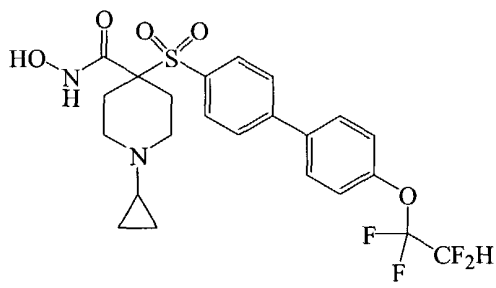
(60-1),



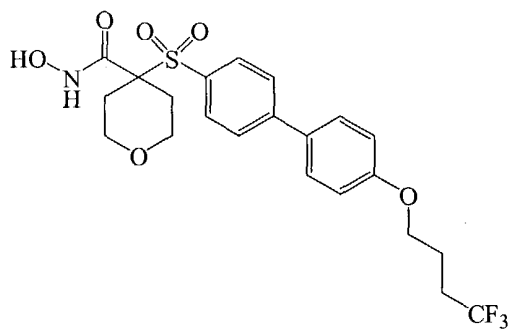
(60-2),



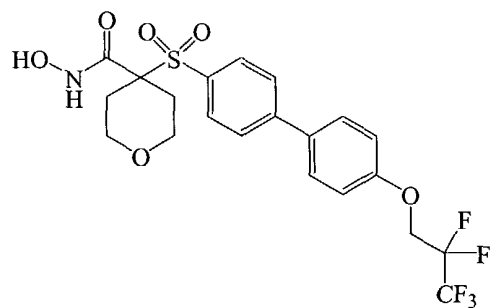
(60-3),



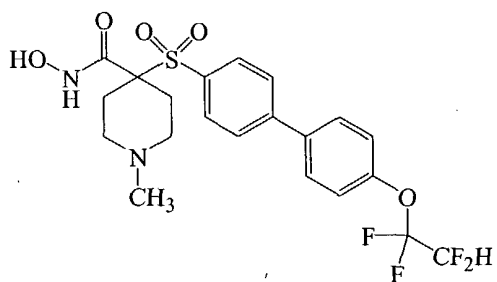
(60-4),



(60-5),



(60-6), and

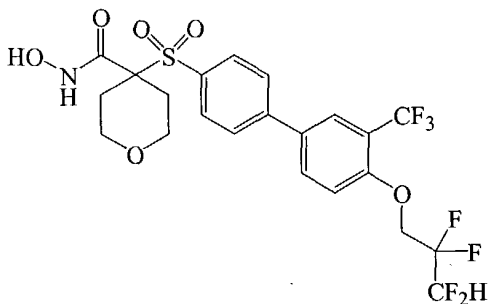


(60-7).

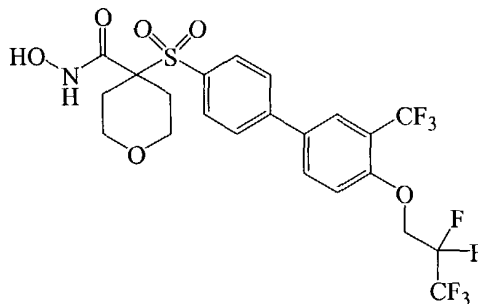
61. A compound or salt thereof according to claim 58, wherein E<sup>2</sup> is phenyl substituted with one or more substituents independently selected from the group consisting of halogen and haloalkyl.

5

62. A compound or salt thereof according to claim 61, wherein the compound is selected from the group consisting of:



(62-1), and

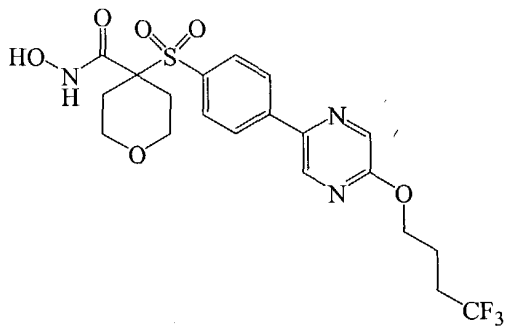


(62-2).

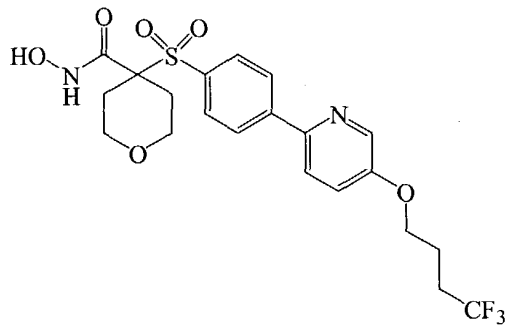
63. A compound or salt thereof according to claim 58, wherein E<sup>2</sup> is selected from the group consisting of pyridinyl, pyrazinyl, and pyrimidinyl.

10

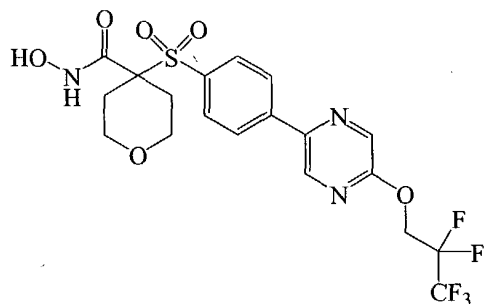
64. A compound or salt thereof according to claim 63, wherein the compound is selected from the group consisting of:



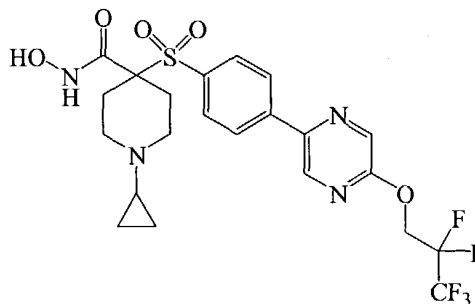
(64-1),



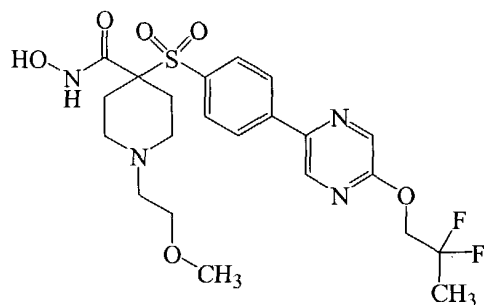
(64-2),



(64-3),



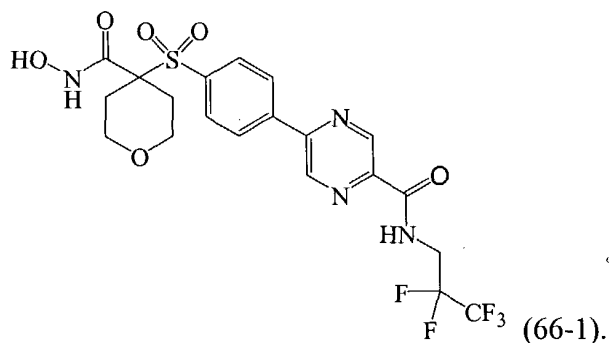
(64-4), and



(64-5).

65. A compound or salt thereof according to claim 49, wherein E<sup>3</sup> is -C(O)-N(H)-.

- 5            66. A compound or salt thereof according to claim 65, wherein the compound corresponds in structure to Formula (66-1):



(66-1).

- 10           67. A compound or salt thereof according to claim 12, wherein E<sup>4</sup> is selected from the group consisting of alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl,

aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein any such group:

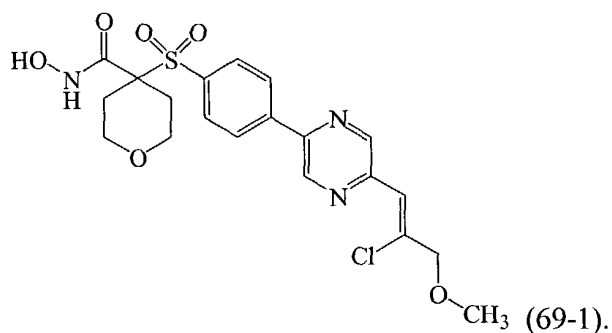
comprises at least two carbon atoms, and

is substituted with one or more independently selected halogen, and

5 is optionally substituted with one or more independently selected R<sup>d</sup> substituents.

68. A compound or salt thereof according to claim 67, wherein E<sup>3</sup> is a bond.

10 69. A compound or salt thereof according to claim 68, wherein the compound corresponds in structure to Formula (69-1):

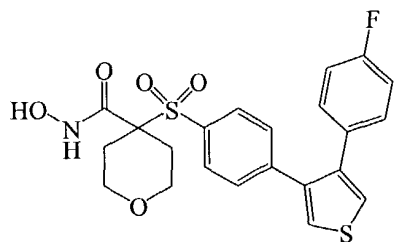


15 70. A compound or salt thereof according to claim 67, wherein E<sup>4</sup> is phenyl substituted with one or more substituents selected from the group consisting of halogen, haloalkyl, and haloalkoxy.

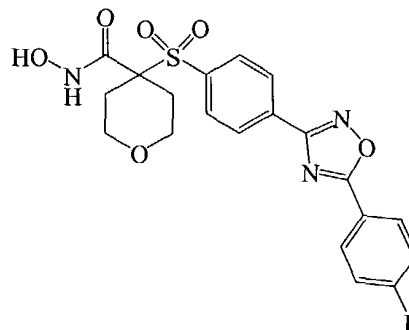
71. A compound or salt thereof according to claim 70, wherein E<sup>3</sup> is a bond.

20 72. A compound or salt thereof according to claim 71, wherein E<sup>2</sup> is selected from the group consisting of oxadiazolyl, thienyl, and pyridinyl.

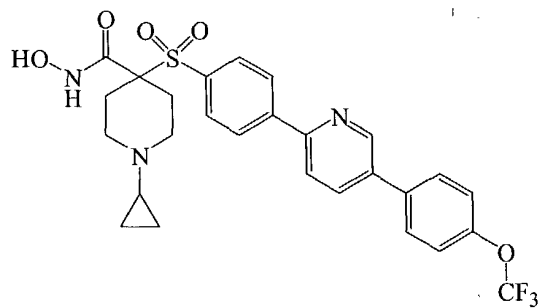
73. A compound or salt thereof according to claim 72, wherein the compound is selected from the group consisting of:



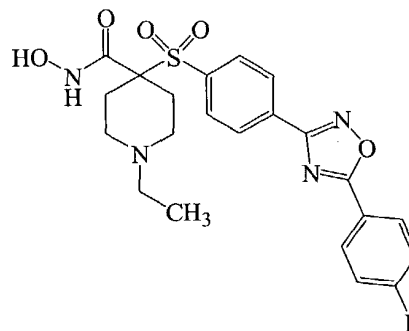
(73-1),



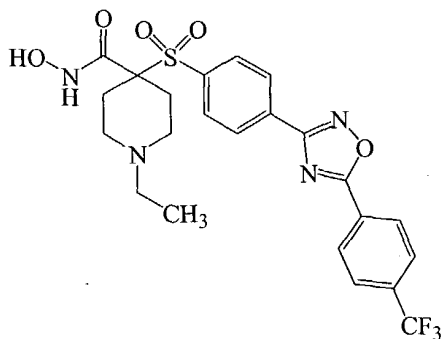
(73-2),



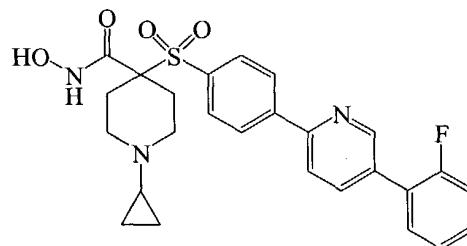
(73-3),



(73-4),



(73-5), and

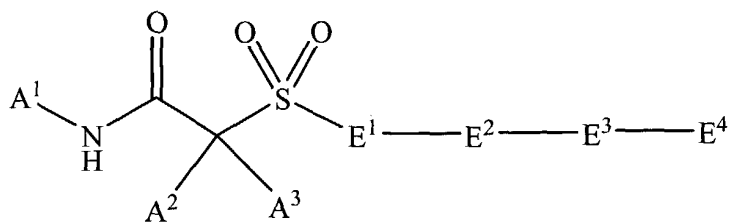


(73-6).

74. A salt according to claim 1, wherein the salt comprises HCl or  $\text{CF}_3\text{-C(O)-OH}$ .

5

75. A compound or a salt thereof, wherein:  
the compound corresponds in structure to Formula (75-1):



$A^1$  is selected from the group consisting of hydrogen, hydroxy, carbocycloxy, and heterocycloxy; and

as to  $A^2$  and  $A^3$ :

5            $A^2$  and  $A^3$ , together with the carbon to which they are bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected  $R^X$  substituents, and

10           the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected  $R^X$  substituents, or

15            $A^2$  and  $A^3$  are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocycloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected  $R^X$  substituents, and

25           any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the heterocyclyl and carbocyclyl optionally are  
substituted with up to 3 independently selected R<sup>x</sup> substituents;  
and

E<sup>1</sup> is aryl optionally substituted with one or more independently selected R<sup>x</sup>  
5 substituents; and

E<sup>2</sup> is selected from the group consisting of aryl and heteroaryl, wherein:

the aryl or heteroaryl optionally substituted with one or more  
independently selected R<sup>x</sup> substituents; and

E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-,  
10 -N(R<sup>b</sup>)-, -C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-,  
-S-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-,  
-C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-, alkyl,  
alkenyl, carbonylalkyl, and alkylcarbonyl, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is  
15 substituted with one or more independently selected R<sup>c</sup> substituents; and

E<sup>4</sup> is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxyalkyl,  
alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl,  
alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl,  
carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl,

20 wherein any such group:

is substituted with one or more independently-selected halogen, and

is optionally substituted with one or more independently selected R<sup>d</sup>  
substituents; and

each R<sup>x</sup> is independently selected from the group consisting of halogen, cyano,  
25 hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,  
R<sup>b</sup>-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl,  
R<sup>b</sup>R<sup>b</sup>-aminoalkoxy, R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl,  
carbocyclylloxy, carbocyclylloxyalkoxy, carbocyclylthio, heterocyclyl,  
heterocyclylalkyl, heterocyclylloxy, heterocyclylloxyalkoxy, heterocyclylthio,  
30 alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl,  
alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl,

carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl,  
carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl,  
carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl,  
heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl,  
5 heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl,  
aminosulfonylalkyl, and  $-R^{x1}-R^{x2}$ , wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
10 alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are  
substituted with one or more substituents independently selected from  
the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently  
15 selected alkyl; and

each  $R^{x1}$  is independently selected from the group consisting of  $-C(O)-$ ,  $-C(S)-$ ,  
 $-C(NR^y)-$ , and  $-S(O)_2-$ ; and

each  $R^y$  is independently selected from the group consisting of hydrogen and  
hydroxy; and

20 each  $R^{x2}$  is independently selected from the group consisting of hydrogen,  
hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy,  $R^b$ -oxyalkyl,  
alkenyloxy, alkynyloxy,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  
 $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocyclyoxy,  
carbocyclyoxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyoxy, and  
25 heterocyclyoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl,  
alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R<sup>b</sup> is independently selected from the group consisting of hydrogen,

5 hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocycloxyalkyl,  
10 heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

15 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R<sup>c</sup> is independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino,  
20 di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

25 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R<sup>d</sup> is independently selected from the group consisting of halogen,

hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, -N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>e</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

30 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl,  
carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

5           any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino; and

each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl,  
10   -O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclalkyl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino; and

15       each R<sup>h</sup> is independently selected from the group consisting of hydrogen, alkyl,  
carbocyclyl, carbocyclalkyl, heterocyclyl, and heterocyclalkyl, wherein:

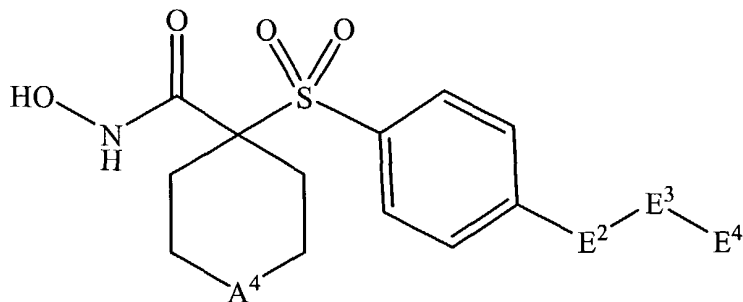
any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
20   aminocarbonyl, and amino.

76. A compound or salt thereof according to claim 75, wherein E<sup>1</sup> is phenyl.

77. A compound or salt thereof according to claim 76, wherein A<sup>1</sup> is hydroxy.

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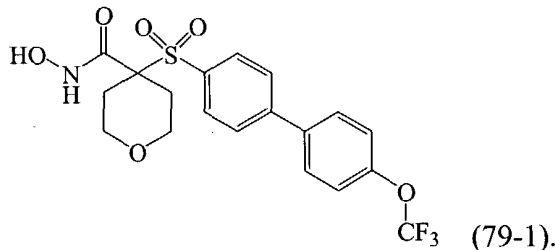
78. A compound or salt thereof according to claim 77, wherein:  
the compound corresponds in structure to Formula (78-1):



(78-1); and

A<sup>4</sup> is selected from the group consisting of -O-, -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-.

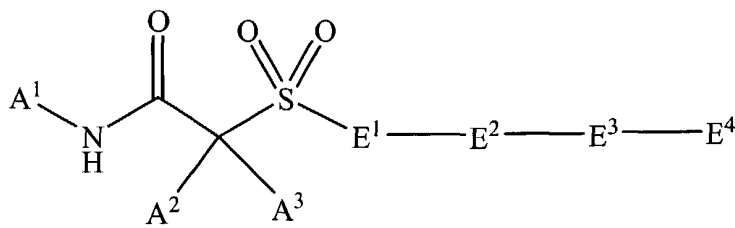
- 5            79. A compound or salt thereof according to claim 78, wherein the compound corresponds in structure to Formula (79-1):



(79-1).

80. A compound or a salt thereof, wherein:

- 10           the compound corresponds in structure to Formula (80-1):



(80-1); and

A<sup>1</sup> is selected from the group consisting of hydrogen, hydroxy, carbocycloxy, and heterocycloxy; and

as to A<sup>2</sup> and A<sup>3</sup>:

- 15           A<sup>2</sup> and A<sup>3</sup>, together with the carbon to which they are bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn,

5 optionally substituted with up to 3 independently selected R<sup>x</sup> substituents, or

A<sup>2</sup> and A<sup>3</sup> are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyoxyalkyl, 10 carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyoxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

15 any member of such group optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

20 the heterocyclyl and carbocyclyl optionally are substituted with up to 3 independently selected R<sup>x</sup> substituents; and

E<sup>1</sup> is aryl optionally substituted with one or more independently selected R<sup>x</sup> substituents; and

25 E<sup>2</sup> is selected from the group consisting of aryl and heteroaryl, wherein the aryl or heteroaryl is:

substituted with one or more independently selected halogen, and optionally substituted with one or more independently selected R<sup>x</sup> substituents; and

30 E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, -N(R<sup>b</sup>)-, -C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-,

-S-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-, -C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-, alkyl, alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R<sup>c</sup> substituents; and

E<sup>4</sup> is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl,

wherein:

any such group optionally is substituted with one or more independently selected R<sup>d</sup> substituents; and

-E<sup>3</sup>-E<sup>4</sup> comprises at least two non-hydrogen atoms; and

each R<sup>x</sup> is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R<sup>b</sup>-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy, R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and -R<sup>x1</sup>-R<sup>x2</sup>, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently selected alkyl; and

each  $R^{x1}$  is independently selected from the group consisting of  $-C(O)-$ ,  $-C(S)-$ ,  $-C(NR^y)-$ , and  $-S(O)_2-$ ; and

each  $R^y$  is independently selected from the group consisting of hydrogen and hydroxy; and

each  $R^{x2}$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy,  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocycliloxy, carbocycliloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocycliloxy, and

heterocycliloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each  $R^b$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocycliloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocycliloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

5 each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

10 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R<sup>d</sup> is independently selected from the group consisting of halogen, 15 hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, -N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>e</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, 20 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, 25 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl, -O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclylalkyl, and heterocyclylalkyl, wherein:

30 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>h</sup> independently selected from the group consisting of hydrogen, alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

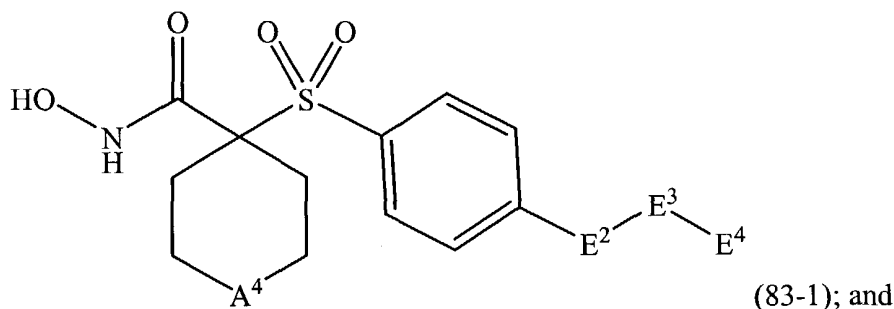
- 5           any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

10           81. A compound or salt thereof according to claim 80, wherein E<sup>1</sup> is phenyl.

82. A compound or salt thereof according to claim 81, wherein A<sup>1</sup> is hydroxy.

83. A compound or salt thereof according to claim 82, wherein:

15           the compound corresponds in structure to Formula (83-1):



A<sup>4</sup> is selected from the group consisting of -O-, -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-.

20           84. A compound or salt thereof according to claim 83, wherein E<sup>2</sup> is selected from the group consisting of aryl and heteroaryl, wherein:

the aryl or heteroaryl is substituted with one halogen.

85. A compound or salt thereof according to claim 84, wherein E<sup>2</sup> is selected  
25           from the group consisting of aryl and heteroaryl, wherein:

the aryl or heteroaryl is substituted with one fluoro.

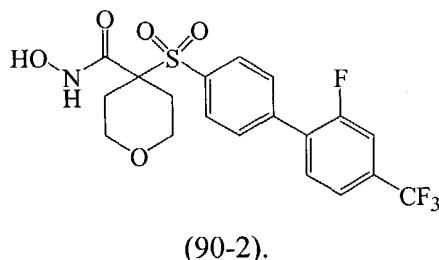
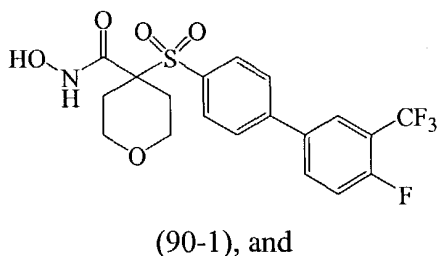
86. A compound or salt thereof according to claim 84, wherein E<sup>2</sup> is phenyl substituted with one halogen.

87. A compound or salt thereof according to claim 86, wherein E<sup>2</sup> is phenyl substituted with one fluoro.

88. A compound or salt thereof according to claim 84, wherein -E<sup>3</sup>-E<sup>4</sup> is halo-C<sub>1</sub>-C<sub>6</sub>-alkyl.

89. A compound or salt thereof according to claim 88, wherein -E<sup>3</sup>-E<sup>4</sup> is trifluoromethyl.

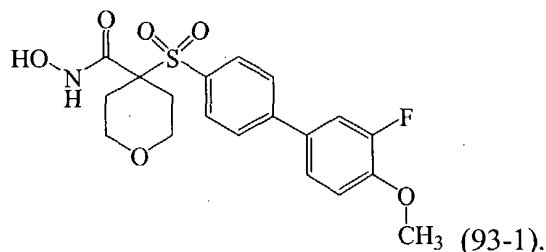
90. A compound or salt thereof according to claim 89, wherein the compound is selected from the group consisting of:



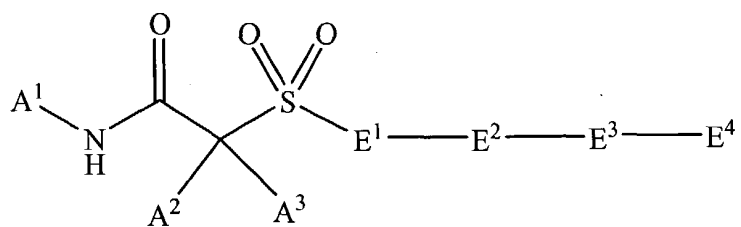
91. A compound or salt thereof according to claim 84, wherein -E<sup>3</sup>-E<sup>4</sup> is C<sub>1</sub>-C<sub>6</sub>-alkoxy.

92. A compound or salt thereof according to claim 91, wherein -E<sup>3</sup>-E<sup>4</sup> is methoxy.

93. A compound or salt thereof according to claim 92, wherein the compound corresponds in structure to Formula (93-1):



94. A compound or a salt thereof, wherein:  
the compound corresponds in structure to Formula (94-1):



A<sup>1</sup> is selected from the group consisting of hydrogen, hydroxy, carbocycloxy,  
and heterocycloxy; and

as to A<sup>2</sup> and A<sup>3</sup>:

A<sup>2</sup> and A<sup>3</sup>, together with the carbon to which they are bonded, form  
heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up  
to 3 independently selected R<sup>x</sup> substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two  
substituents such that the two substituents, together with the atom(s) to  
which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn,  
optionally substituted with up to 3 independently selected R<sup>x</sup>  
substituents, or

A<sup>2</sup> and A<sup>3</sup> are independently selected from the group consisting of  
hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl,  
carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocycloxyalkyl,  
carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl,  
carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl,

heterocyclalkynyl, heterocycloxyalkyl, heterocyclalkoxyalkyl,  
heterocyclalkylthio, heterocyclthioalkyl, and heterocyclalkylthioalkyl,  
wherein:

any member of such group optionally is substituted with up to 3  
independently selected R<sup>x</sup> substituents, and

any member of such group optionally is substituted with two  
substituents such that the two substituents, together with the atom(s) to  
which they are bonded, form a carbocycl or heterocycl, wherein:

the heterocycl and carbocycl optionally are

substituted with up to 3 independently selected R<sup>x</sup> substituents;  
and

E<sup>1</sup> is aryl optionally substituted with one or more independently selected R<sup>x</sup>  
substituents; and

E<sup>2</sup> is selected from the group consisting of aryl and heteroaryl, wherein:

the aryl or heteroaryl optionally substituted with one or more  
independently selected R<sup>x</sup> substituents; and

E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-O-, -O-C(O)-, -N(R<sup>b</sup>)-,  
-C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-, -S-,  
-S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-,  
-C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-,  
alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is  
substituted with one or more independently selected R<sup>c</sup> substituents; and

E<sup>4</sup> is selected from the group consisting of hydroxyalkyl, alkenyl, alkynyl,  
alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl,  
alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, carbocycl, carbocyclalkyl,  
carbocyclalkoxyalkyl, heterocycl, and heterocyclalkoxyalkyl, wherein:

any such group optionally is substituted with one or more independently  
selected R<sup>d</sup> substituents; and

each R<sup>x</sup> is independently selected from the group consisting of halogen, cyano,  
hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,

$R^b$ -oxyalkyl, alkenyloxy, alkynyloxy, alkylthio,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, 5 alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, 10 heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and  $-R^{x1}-R^{x2}$ , wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, 15 hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and 20

the amino optionally is substituted with up to 2 independently selected alkyl; and

each  $R^{x1}$  is independently selected from the group consisting of  $-C(O)-$ ,  $-C(S)-$ ,  $-C(NR^y)-$ , and  $-S(O)_2-$ ; and

each  $R^y$  is independently selected from the group consisting of hydrogen and 25 hydroxy; and

each  $R^{x2}$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy,  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, and 30 heterocyclyloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

5                   the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R<sup>b</sup> is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, 10 alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, 15 heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, 20 alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and 25 heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

30                   each R<sup>d</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl,

$-N(R^e)(R^e)$ ,  $-C(O)(R^e)$ ,  $-S-R^e$ ,  $-S(O)_2-R^e$ , carbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each  $R^e$  is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each  $R^e$  is independently selected from the group consisting of hydrogen, alkyl,  $-O-R^h$ ,  $-N(R^h)(R^h)$ , carbocyclalkyl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

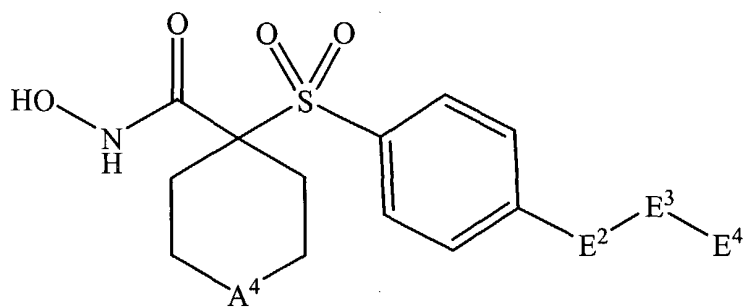
each  $R^h$  is independently selected from the group consisting of hydrogen, alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

95. A compound or salt thereof according to claim 94, wherein  $E^1$  is phenyl.

96. A compound or salt thereof according to claim 95, wherein  $A^1$  is hydroxy.

97. A compound or salt thereof according to claim 96, wherein:  
the compound corresponds in structure to Formula (97-1):

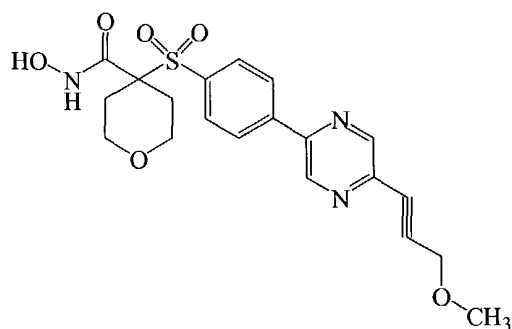


$A^4$  is selected from the group consisting of -O-, -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-.

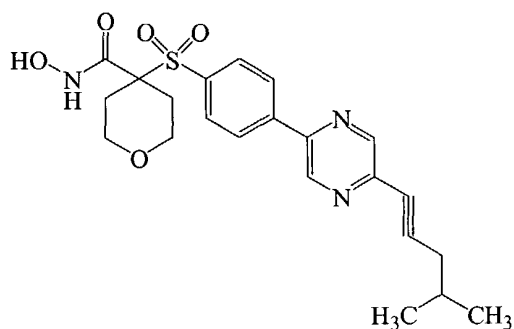
98. A compound or salt thereof according to claim 97, wherein E<sup>3</sup> is a bond.

99. A compound or salt thereof according to claim 98, wherein E<sup>4</sup> is alkynyl optionally substituted with alkoxy.

100. A compound or salt thereof according to claim 99, wherein the compound is selected from the group consisting of:



(100-1), and



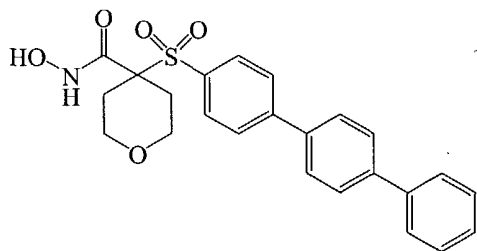
(100-2).

101. A compound or salt thereof according to claim 98, wherein E<sup>4</sup> is selected from the group consisting of carbocyclyl and carbocyclylalkyl, wherein:

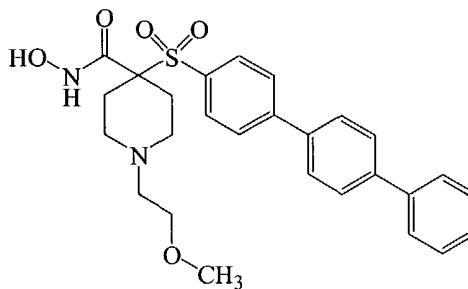
the carbocyclyl or carbocyclylalkyl optionally is substituted with one or more substituents independently selected from alkoxy and oxo.

102. A compound or salt thereof according to claim 101, wherein E<sup>2</sup> is phenyl.

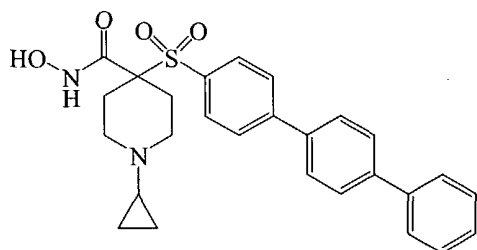
103. A compound or salt thereof according to claim 102, wherein the compound is selected from the group consisting of:



(103-1),



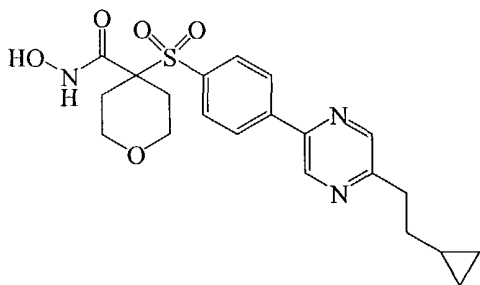
(103-2), and



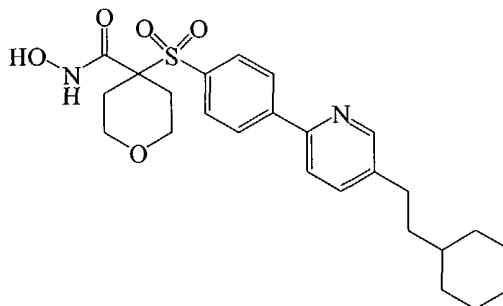
(103-3).

5 104. A compound or salt thereof according to claim 101, wherein E<sup>2</sup> is heteroaryl.

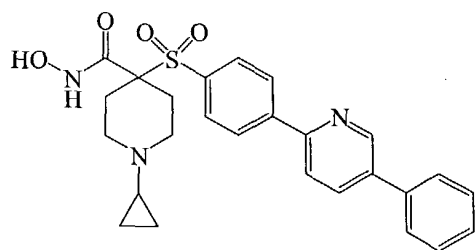
105. A compound or salt thereof according to claim 104, wherein the compound is selected from the group consisting of:



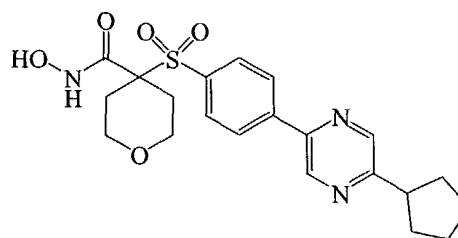
(105-1),



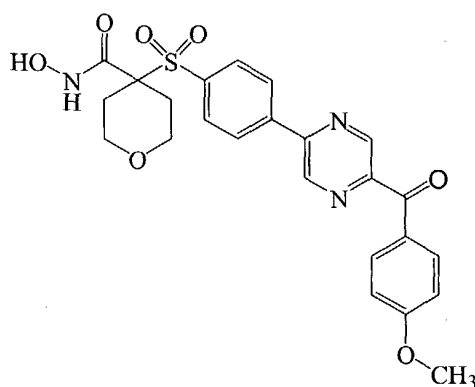
(105-2),



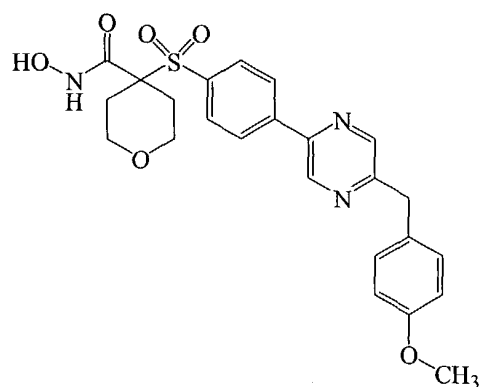
(105-3),



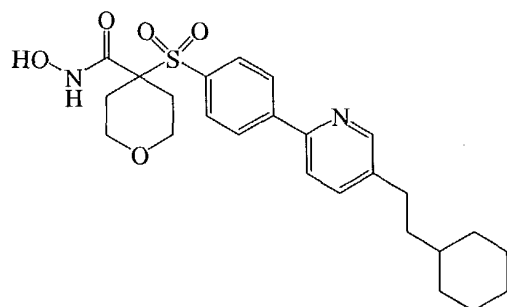
(105-4),



(105-5),



(105-6), and

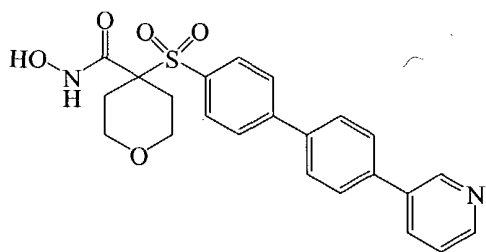


(105-7).

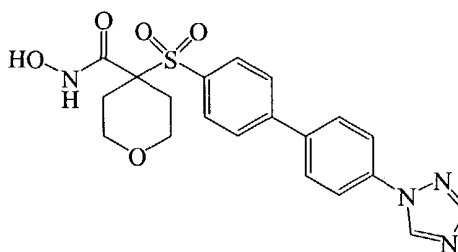
106. A compound or salt thereof according to claim 98, wherein E<sup>4</sup> is heterocyclyl optionally substituted with alkyl.

5 107. A compound or salt thereof according to claim 106, wherein E<sup>2</sup> is phenyl.

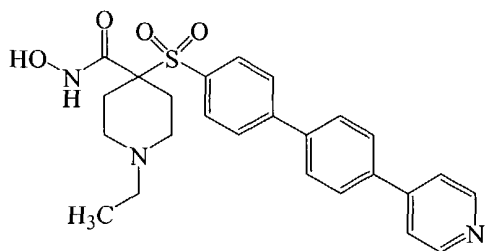
108. A compound or salt thereof according to claim 107, wherein the compound is selected from the group consisting of:



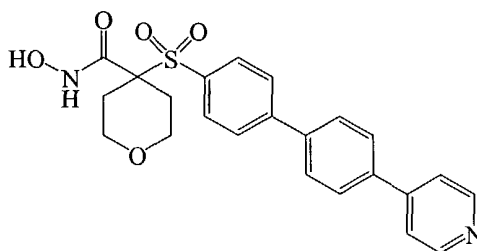
(108-1),



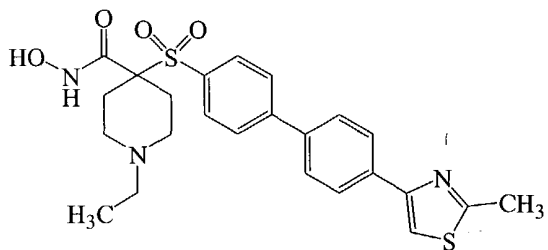
(108-2),



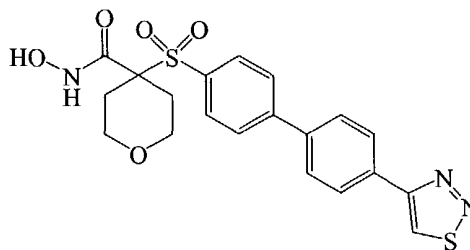
(108-3),



(108-4),



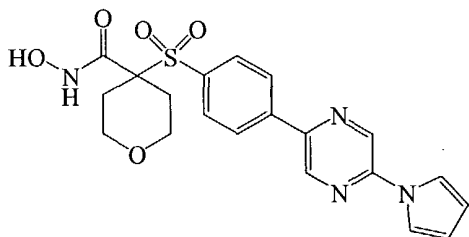
(108-5), and



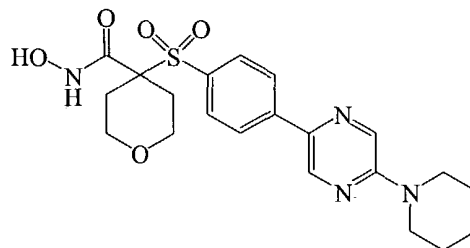
(108-6).

109. A compound or salt thereof according to claim 106, wherein E<sup>2</sup> is heteroaryl.

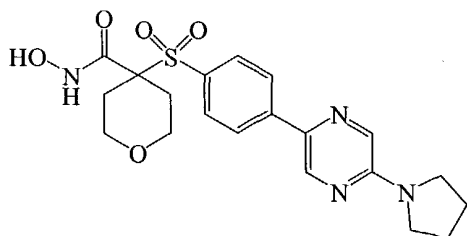
5 110. A compound or salt thereof according to claim 109, wherein the compound is selected from the group consisting of:



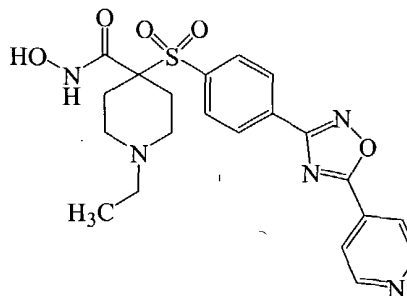
(110-1),



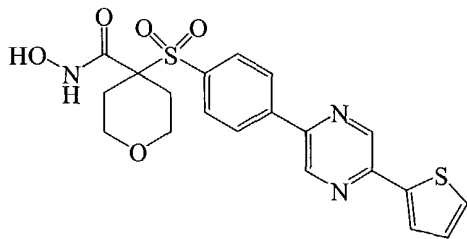
(110-2),



(110-3),



(110-4), and

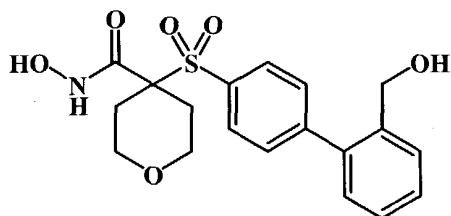


(110-5).

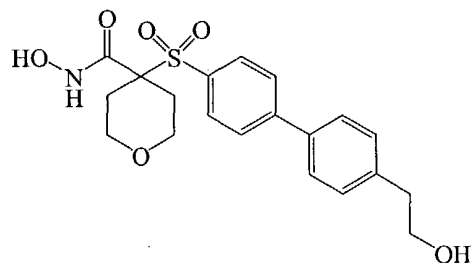
111. A compound or salt thereof according to claim 98, wherein  $E^4$  is selected from the group consisting of hydroxyalkyl and alkoxyalkyl, wherein:  
the hydroxyalkyl or alkoxyalkyl optionally is substituted with oxo.

5

112. A compound or salt thereof according to claim 111, wherein the compound is selected from the group consisting of:



(112-1), and

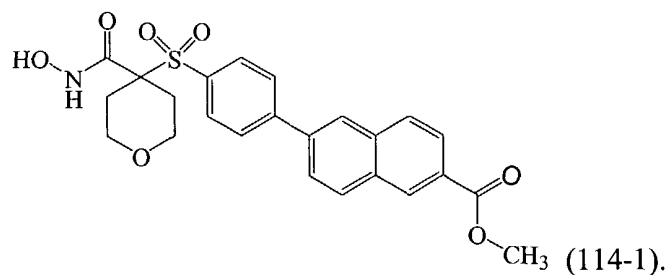


(112-2).

113. A compound or salt thereof according to claim 111, wherein  $E^2$  is  
naphthyl.

10

114. A compound or salt thereof according to claim 113, wherein the compound corresponds in structure to Formula (114-1):

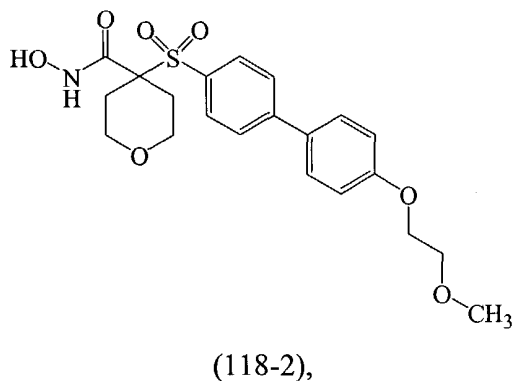
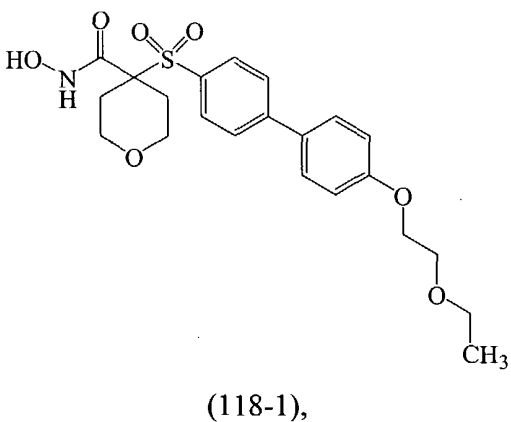


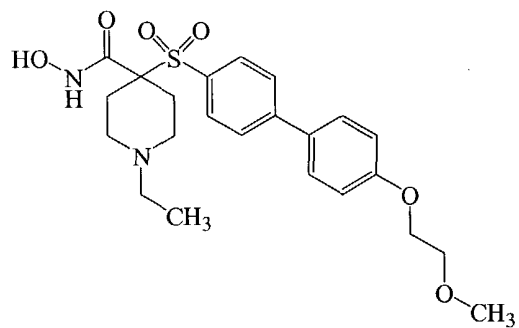
115. A compound or salt thereof according to claim 97, wherein E<sup>3</sup> is -O-.

5        116. A compound or salt thereof according to claim 115, wherein E<sup>4</sup> is selected from the group consisting of hydroxyalkyl, alkoxyalkyl, carbocyclyl, and carbocyclylalkyl.

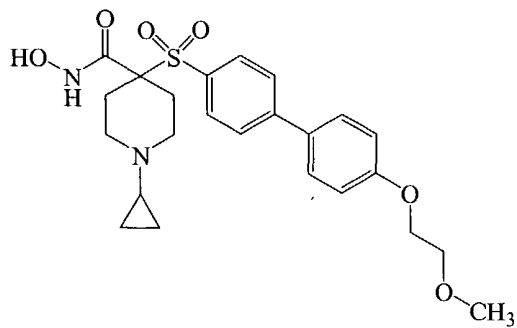
10       117. A compound or salt thereof according to claim 116, wherein E<sup>2</sup> is phenyl optionally substituted with one or more substituents independently selected from the group consisting of halogen and haloalkyl.

118. A compound or salt thereof according to claim 117, wherein the compound is selected from the group consisting of:

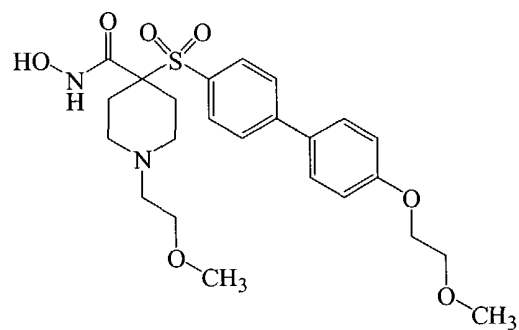




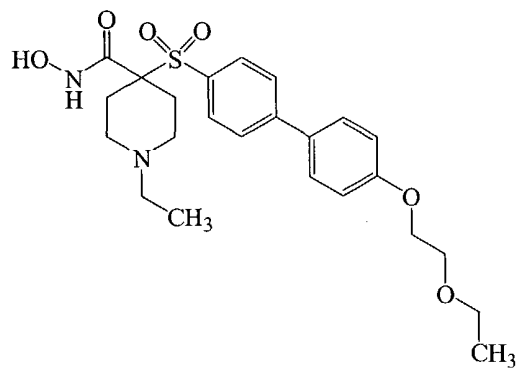
(118-3),



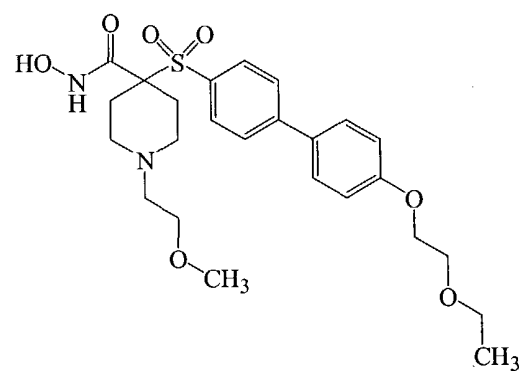
(118-4),



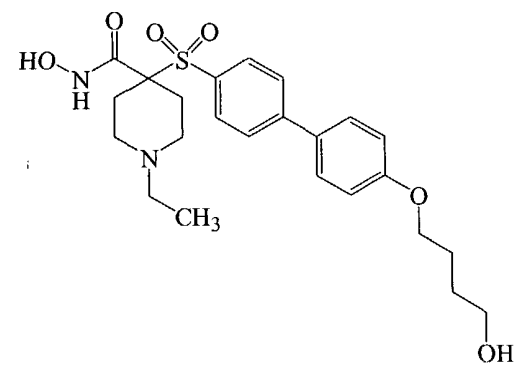
(118-5),



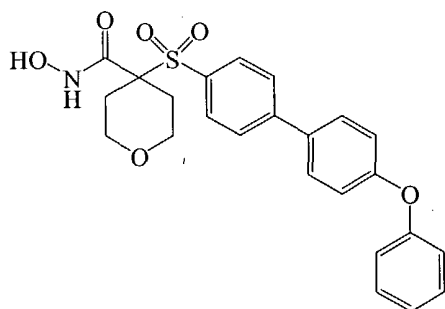
(118-6),



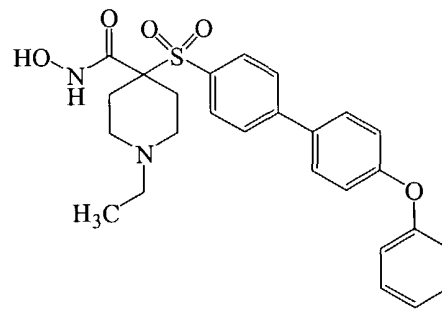
(118-7),



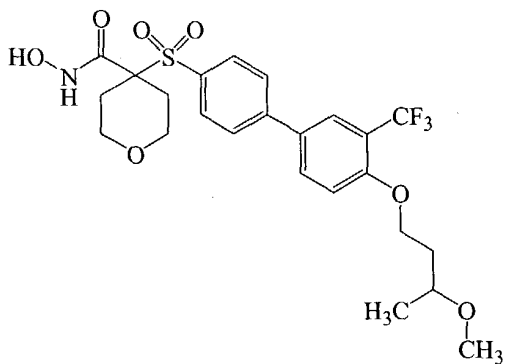
(118-8),



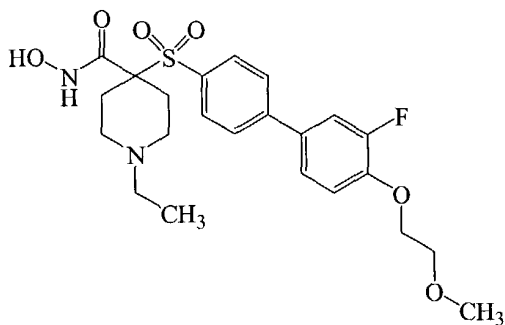
(118-9),



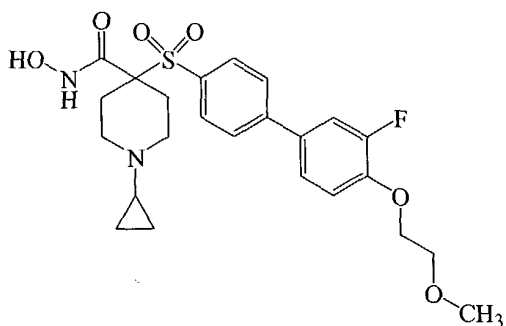
(118-10),



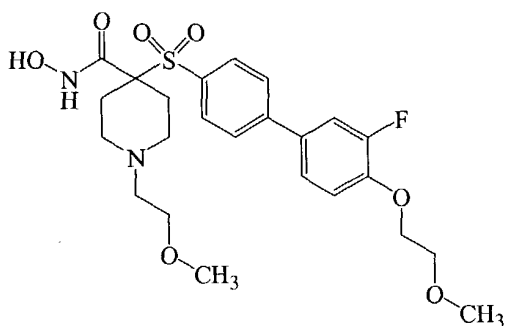
(118-11),



(118-12),



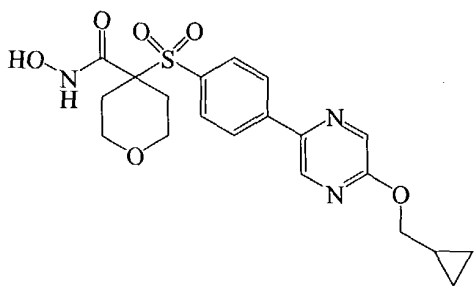
(118-13), and



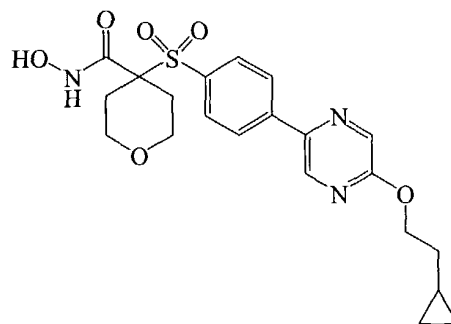
(118-14).

119. A compound or salt thereof according to claim 116, wherein E<sup>2</sup> is heteroaryl.

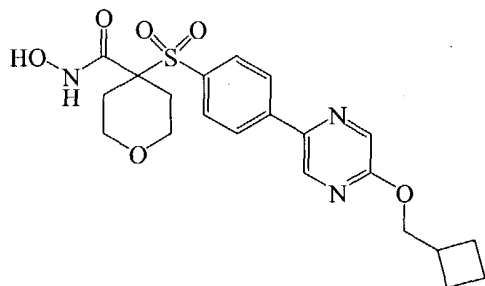
5 120. A compound or salt thereof according to claim 119, wherein the compound is selected from the group consisting of:



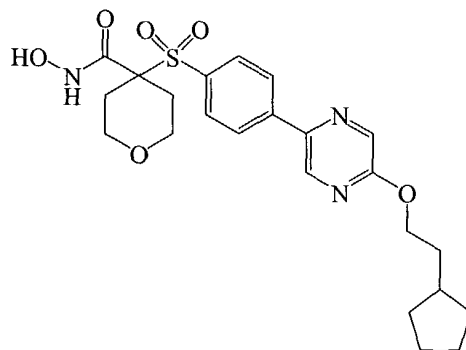
(120-1),



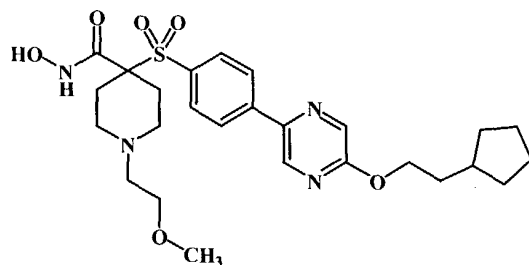
(120-2),



(120-3),



(120-4), and

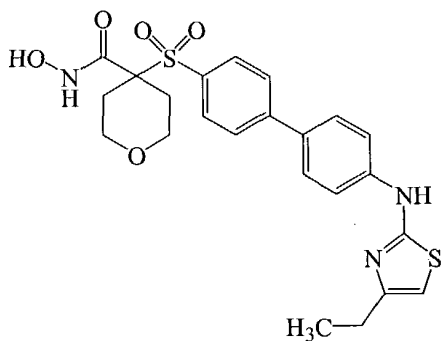


(120-5).

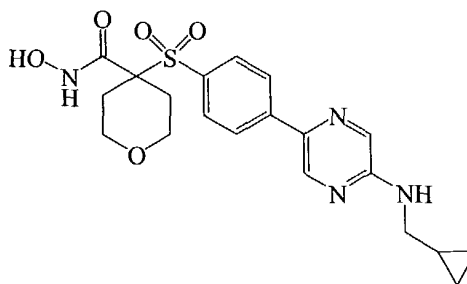
121. A compound or salt thereof according to claim 97, wherein E<sup>3</sup> is -N(H)-.

122. A compound or salt thereof according to claim 121, wherein E<sup>4</sup> is  
5 selected from the group consisting of carbocyclalkyl and alkylheterocycl.

123. A compound or salt thereof according to claim 122, wherein the  
compound is selected from the group consisting of:



(123-1), and

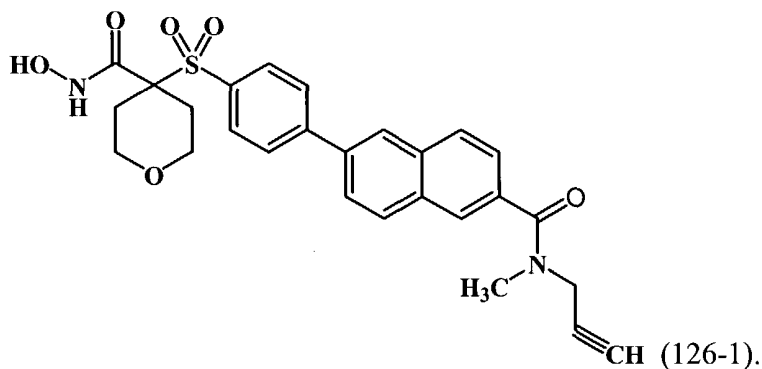


(123-2).

124. A compound or salt thereof according to claim 97, wherein E<sup>3</sup> is selected from the group consisting of -C(O)-N(H)- and -C(O)-N(CH<sub>3</sub>)-.

125. A compound or salt thereof according to claim 124, wherein E<sup>4</sup> is alkynyl.

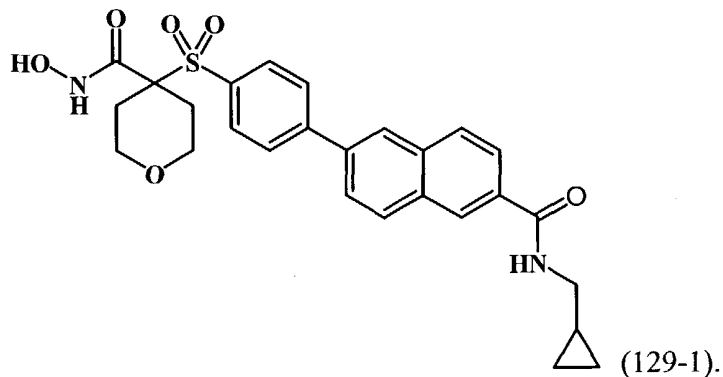
126. A compound or salt thereof according to claim 125, wherein the compound corresponds in structure to Formula (126-1):



127. A compound or salt thereof according to claim 124, wherein E<sup>4</sup> is selected from the group consisting of carbocyclyl and carbocyclylalkyl.

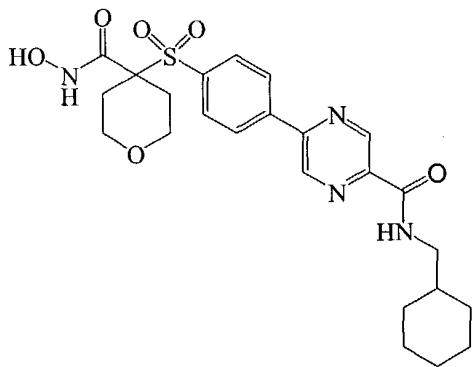
128. A compound or salt thereof according to claim 127, wherein E<sup>2</sup> is aryl.

129. A compound or salt thereof according to claim 128, wherein the compound corresponds in structure to Formula (129-1):

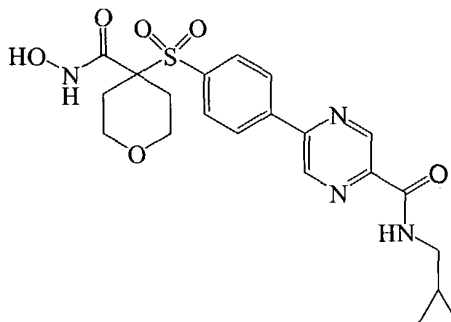


130. A compound or salt thereof according to claim 127, wherein E<sup>2</sup> is heteroaryl.

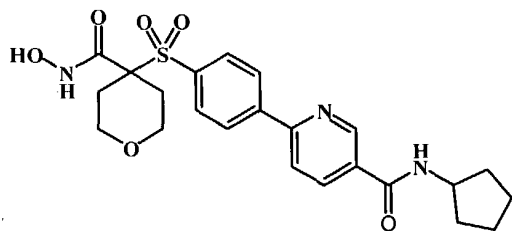
131. A compound or salt thereof according to claim 130, wherein the  
5 compound is selected from the group consisting of:



(131-1),



(131-2), and

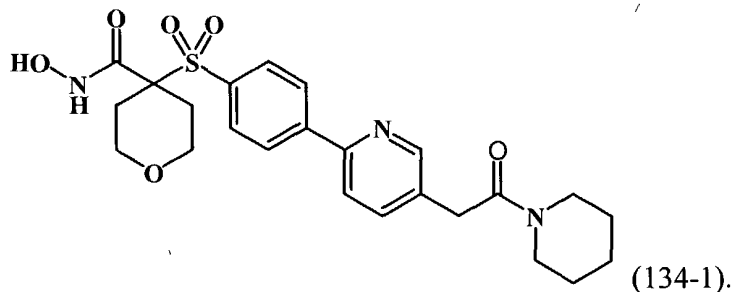


(131-3).

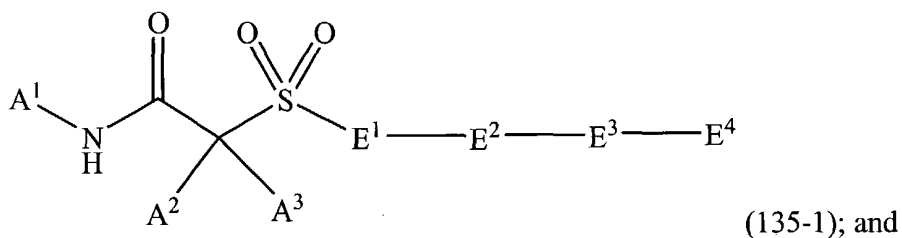
132. A compound or salt thereof according to claim 97, wherein E<sup>3</sup> is carbonylalkyl.

10 133. A compound or salt thereof according to claim 132, wherein E<sup>4</sup> is heterocyclyl.

134. A compound or salt thereof according to claim 133, wherein the compound corresponds in structure to Formula (134-1):



135. A compound or a salt thereof, wherein:  
the compound corresponds in structure to Formula (135-1):



A<sup>1</sup> is selected from the group consisting of hydrogen, hydroxy, carbocycloxy,  
and heterocycloxy; and

as to A<sup>2</sup> and A<sup>3</sup>:

A<sup>2</sup> and A<sup>3</sup>, together with the carbon to which they are bonded, form  
heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up  
to 3 independently selected R<sup>x</sup> substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two  
substituents such that the two substituents, together with the atom(s) to  
which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn,  
optionally substituted with up to 3 independently selected R<sup>x</sup>  
substituents, or

A<sup>2</sup> and A<sup>3</sup> are independently selected from the group consisting of  
hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl,  
carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocycloxyalkyl,  
carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl,  
carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl,

heterocyclalkynyl, heterocycloxyalkyl, heterocyclalkoxyalkyl,  
heterocyclalkylthio, heterocyclthioalkyl, and heterocyclalkylthioalkyl,  
wherein:

any member of such group optionally is substituted with up to 3

5 independently selected  $R^x$  substituents, and

any member of such group optionally is substituted with two  
substituents such that the two substituents, together with the atom(s) to  
which they are bonded, form a carbocycl or heterocycl, wherein:

the heterocycl and carbocycl optionally are

10 substituted with up to 3 independently selected  $R^x$  substituents;  
and

$E^1$  is aryl optionally substituted with one or more independently selected  $R^x$   
substituents; and

$E^2$  is selected from the group consisting of aryl and heteroaryl, wherein:

15 the aryl or heteroaryl optionally substituted with one or more  
independently selected  $R^x$  substituents; and

$E^3$  is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-,  
-N( $R^b$ )-, -C(O)-N( $R^b$ )-, -N( $R^b$ )-C(O)-, -C(O)-N( $R^b$ )-N( $R^b$ )-C(O)-, -N( $R^b$ )-C(O)-N( $R^b$ )-,  
-S-, -S(O)-, -S(O)<sub>2</sub>-, -N( $R^b$ )-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N( $R^b$ )-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-,  
20 -C(NOH)-, -N( $R^b$ )-C(NH)-, -N( $R^b$ )-C(NOH)-, -C(NH)-N( $R^b$ )-, -C(NOH)-N( $R^b$ )-,  
alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is  
substituted with one or more independently selected  $R^c$  substituents; and

$E^4$  is alkyl, wherein the alkyl:

25 comprises a carbon chain of at least 4 carbon atoms, and

is optionally substituted with one or more independently selected  $R^d$   
substituents; and

each  $R^x$  is independently selected from the group consisting of halogen, cyano,  
hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,

30  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy, alkylthio,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  
 $R^bR^b$ -aminoalkoxy,  $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocycl, carbocyclalkyl,

carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl,  
heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio,  
alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl,  
alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl,  
5 carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl,  
carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl,  
carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl,  
heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl,  
heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl,  
10 aminosulfonylalkyl, and  $-R^{x1}-R^{x2}$ , wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

15 the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are  
substituted with one or more substituents independently selected from  
the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently  
selected alkyl; and

20 each  $R^{x1}$  is independently selected from the group consisting of  $-C(O)-$ ,  $-C(S)-$ ,  
 $-C(NR^y)-$ , and  $-S(O)_2-$ ; and

each  $R^y$  is independently selected from the group consisting of hydrogen and  
hydroxy; and

each  $R^{x2}$  is independently selected from the group consisting of hydrogen,  
25 hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy,  $R^b$ -oxyalkyl,  
alkenyloxy, alkynyloxy,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  
 $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy,  
carbocyclyloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, and  
heterocyclyloxyalkoxy, wherein:

30 any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from

5 the group consisting of halogen and hydroxy; and

each R<sup>b</sup> is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

15 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

25 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R<sup>d</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, -N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>e</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

5 each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

10 each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl, -O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclalkyl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

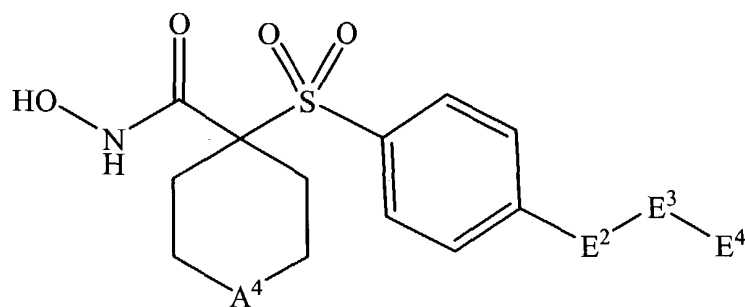
15 each R<sup>h</sup> is independently selected from the group consisting of hydrogen, alkyl, carbocyclyl, carbocyclalkyl, heterocyclyl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

25 136. A compound or salt thereof according to claim 135, wherein E<sup>i</sup> is phenyl.

137. A compound or salt thereof according to claim 136, wherein A<sup>i</sup> is hydroxy.

30 138. A compound or salt thereof according to claim 137, wherein:  
the compound corresponds in structure to Formula (138-1):



(138-1); and

$A^4$  is selected from the group consisting of -O-, -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-.

139. A compound or salt thereof according to claim 138, wherein  $E^4$  is -(CH<sub>2</sub>)<sub>3</sub>-CH<sub>3</sub>.

140. A compound or salt thereof according to claim 138, wherein  $E^4$  is -(CH<sub>2</sub>)<sub>4</sub>-CH<sub>3</sub>.

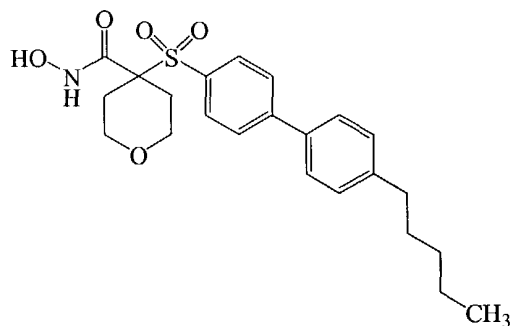
10

141. A compound or salt thereof according to claim 138, wherein  $E^3$  is a bond.

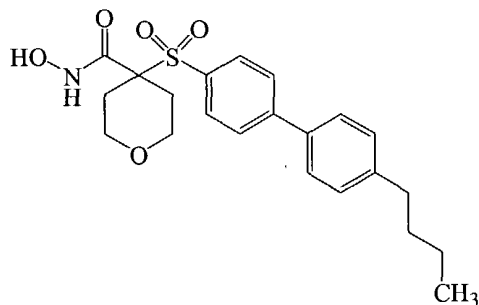
142. A compound or salt thereof according to claim 141, wherein  $E^2$  is phenyl optionally substituted with one or more independently selected halogen.

15

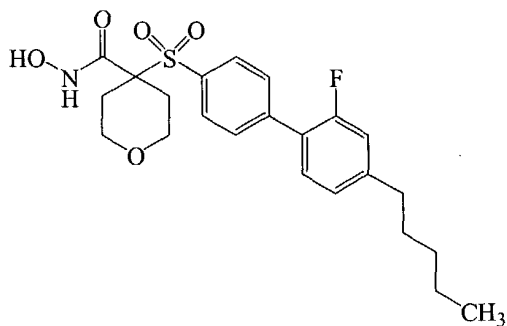
143. A compound or salt thereof according to claim 142, wherein the compound is selected from the group consisting of:



(143-1),



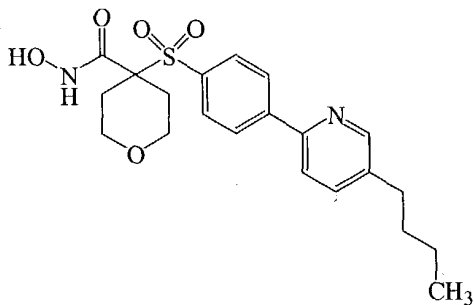
(143-2), and



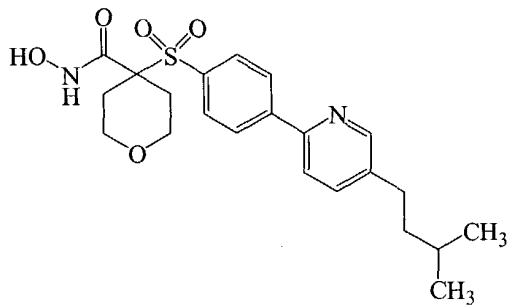
(143-3).

144. A compound or salt thereof according to claim 141, wherein E<sup>2</sup> is heteroaryl.

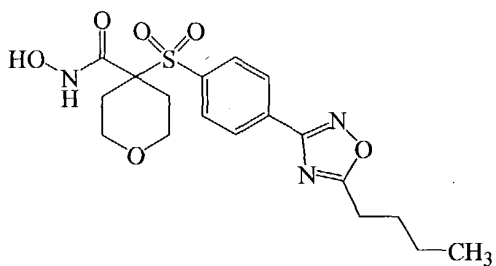
5 145. A compound or salt thereof according to claim 144, wherein the compound is selected from the group consisting of:



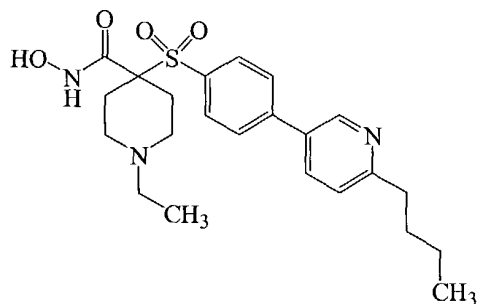
(145-1),



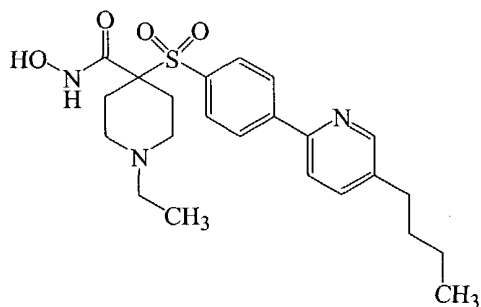
(145-2),



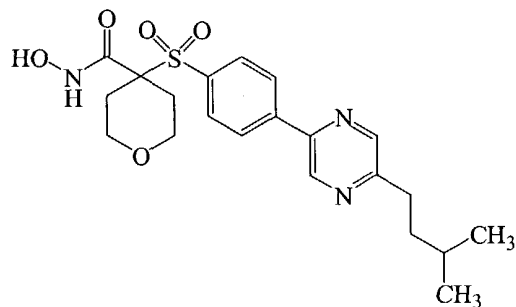
(145-3),



(145-4),



(145-5), and

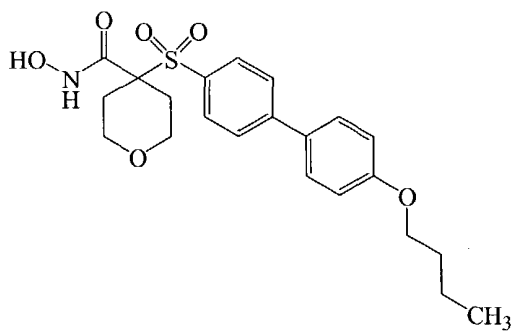


(145-6).

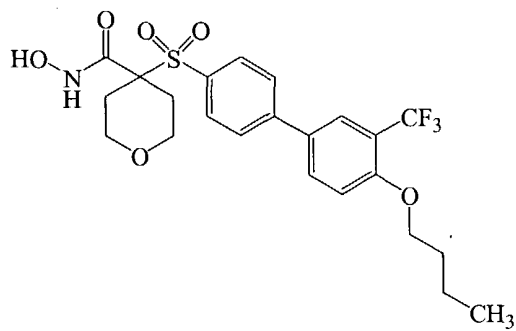
146. A compound or salt thereof according to claim 138, wherein E<sup>3</sup> is -O-.

147. A compound or salt thereof according to claim 146, wherein E<sup>2</sup> is  
5 phenyl optionally substituted with one or more independently selected haloalkyl.

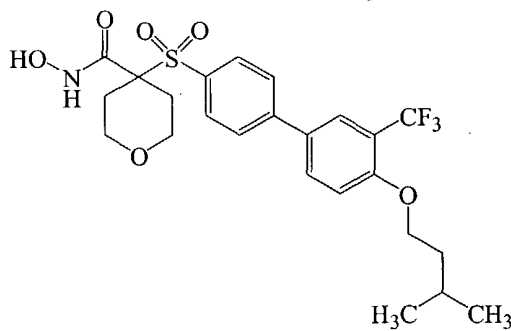
148. A compound or salt thereof according to claim 147, wherein the  
compound is selected from the group consisting of:



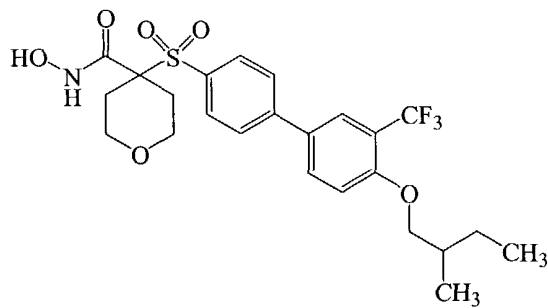
(148-1),



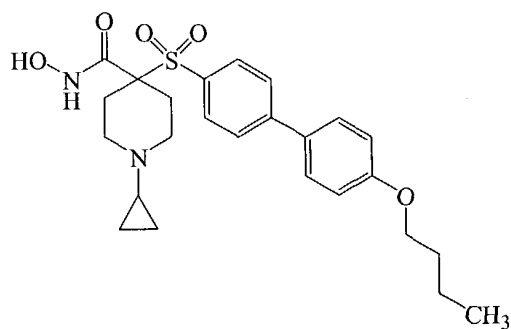
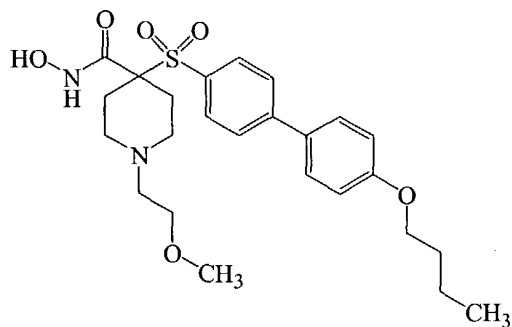
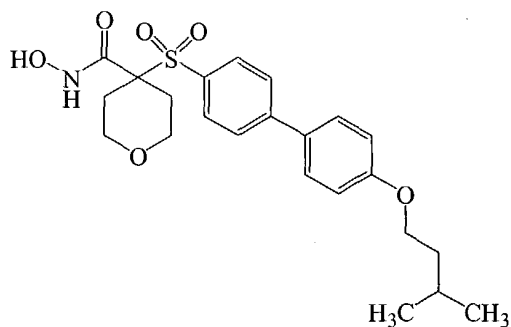
(148-2),



(148-3),

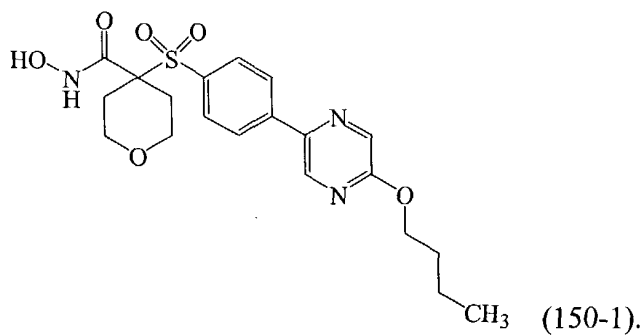


(148-4),



149. A compound or salt thereof according to claim 146, wherein E<sup>2</sup> is heteroaryl.

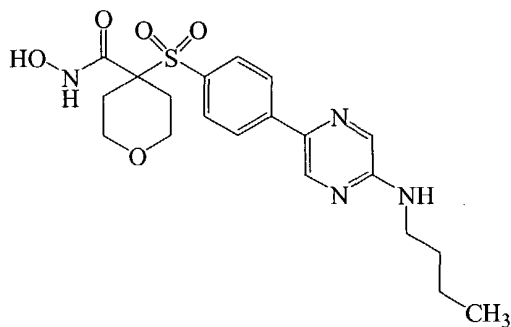
150. A compound or salt thereof according to claim 149, wherein the compound corresponds in structure to Formula (150-1):



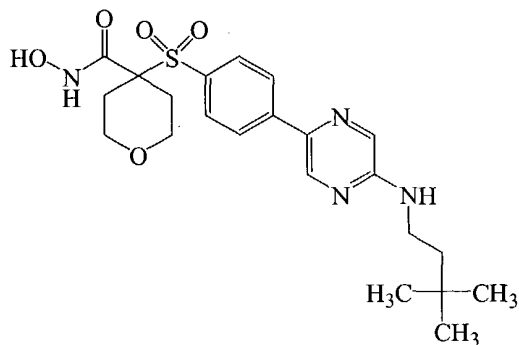
151. A compound or salt thereof according to claim 138, wherein E<sup>3</sup> is -N(H)-.

152. A compound or salt thereof according to claim 151, wherein E<sup>2</sup> is heteroaryl.

153. A compound or salt thereof according to claim 152, wherein the  
5 compound is selected from the group consisting of:



(153-1), and

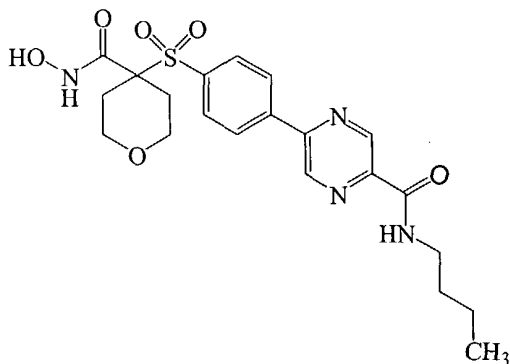


(153-2).

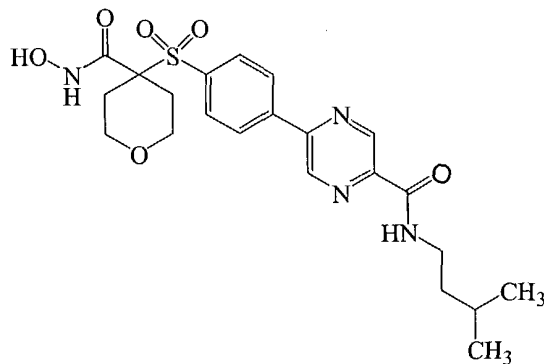
154. A compound or salt thereof according to claim 138, wherein E<sup>3</sup> is -C(O)-N(H)-.

10 155. A compound or salt thereof according to claim 154, wherein E<sup>2</sup> is heteroaryl.

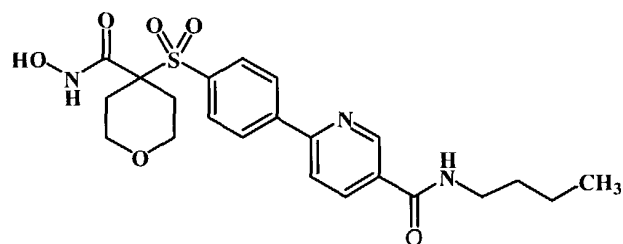
156. A compound or salt thereof according to claim 155, wherein the compound is selected from the group consisting of:



(156-1),

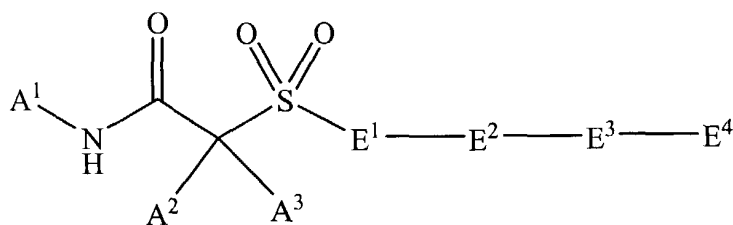


(156-2), and



(156-3).

157. A compound or a salt thereof, wherein:  
the compound corresponds in structure to Formula (157-1):



(157-1); and

$A^1$  is selected from the group consisting of hydrogen, hydroxy, carbocycloxy,  
and heterocycloxy; and

as to  $A^2$  and  $A^3$ :

$A^2$  and  $A^3$ , together with the carbon to which they are bonded, form  
heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up  
to 3 independently selected  $R^X$  substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two  
substituents such that the two substituents, together with the atom(s) to  
which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn,  
optionally substituted with up to 3 independently selected  $R^X$   
substituents, or

$A^2$  and  $A^3$  are independently selected from the group consisting of  
hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl,  
carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocycloxyalkyl,  
carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl,

carbocyclalkylthioalkyl, heterocycl, heterocyclalkyl, heterocyclalkenyl,  
heterocyclalkynyl, heterocycloxyalkyl, heterocyclalkoxyalkyl,  
heterocyclalkylthio, heterocyclthioalkyl, and heterocyclalkylthioalkyl,  
wherein:

5                                   any member of such group optionally is substituted with up to 3  
independently selected R<sup>x</sup> substituents, and

any member of such group optionally is substituted with two  
substituents such that the two substituents, together with the atom(s) to  
which they are bonded, form a carbocycl or heterocycl, wherein:

10                                   the heterocycl and carbocycl optionally are  
substituted with up to 3 independently selected R<sup>x</sup> substituents;  
and

E<sup>1</sup> is aryl optionally substituted with one or more independently selected R<sup>x</sup>  
substituents; and

15                                   E<sup>2</sup> is heteroaryl optionally substituted with one or more independently selected  
R<sup>x</sup> substituents; and

E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-,  
-N(R<sup>b</sup>)-, -C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-,  
-S-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-,  
20 -C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-, alkyl,  
alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is  
substituted with one or more independently selected R<sup>c</sup> substituents; and

E<sup>4</sup> is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxyalkyl,  
25 alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl,  
alkoxyalkylthioalkyl, aminoalkyl, carbocycl, carbocyclalkyl,  
carbocyclalkoxyalkyl, heterocycl, heterocyclalkyl, and heterocyclalkoxyalkyl,  
wherein:

any such group optionally is substituted with one or more independently  
30 selected R<sup>d</sup> substituents; and

each  $R^X$  is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy, alkylthio,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocycliloxy, carbocycliloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocycliloxy, heterocycliloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and  $-R^{x1}-R^{x2}$ , wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently selected alkyl; and

each  $R^{x1}$  is independently selected from the group consisting of  $-C(O)-$ ,  $-C(S)-$ ,  $-C(NR^y)-$ , and  $-S(O)_2-$ ; and

each  $R^y$  is independently selected from the group consisting of hydrogen and hydroxy; and

each  $R^{x2}$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy,  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,

R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocycloxy, carbocycloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocycloxy, and heterocycloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R<sup>b</sup> is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocycloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, amino, alkyl, and carbocyclalkyl; and

each R<sup>d</sup> is independently selected from the group consisting of halogen,  
hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl,  
5 -N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>g</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocycl, alkylcarbocycl,  
carbocyclalkyl, heterocycl, alkylheterocycl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
10 aminocarbonyl, and amino; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl,  
carbocycl, carbocyclalkyl, heterocycl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
15 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino; and

each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl,  
-O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclalkyl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
20 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino; and

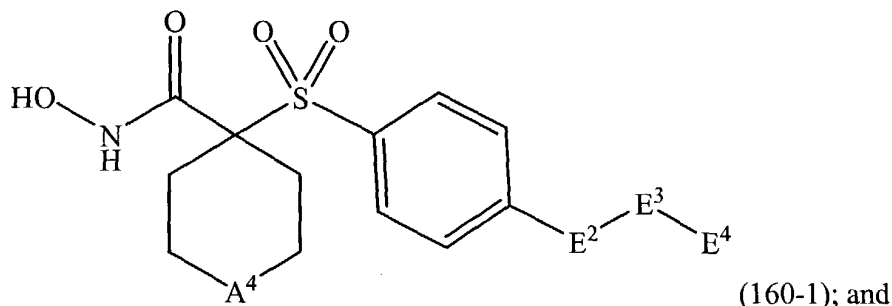
each R<sup>h</sup> is independently selected from the group consisting of hydrogen, alkyl,  
carbocycl, carbocyclalkyl, heterocycl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
25 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino.

158. A compound or salt thereof according to claim 157, wherein E<sup>1</sup> is  
30 phenyl.

159. A compound or salt thereof according to claim 158, wherein A<sup>1</sup> is hydroxy.

160. A compound or salt thereof according to claim 159, wherein:  
the compound corresponds in structure to Formula (160-1):



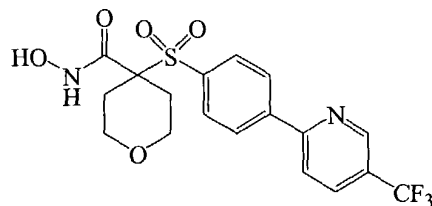
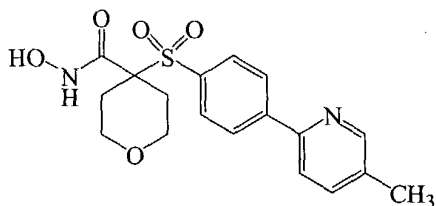
A<sup>4</sup> is selected from the group consisting of -O-, -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-.

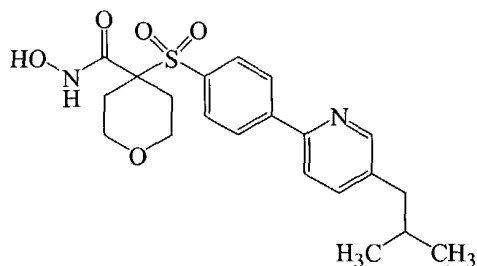
161. A compound or salt thereof according to claim 160, wherein E<sup>2</sup> is 5-member heteroaryl.

162. A compound or salt thereof according to claim 160, wherein E<sup>2</sup> is 6-member heteroaryl.

163. A compound or salt thereof according to claim 162, wherein E<sup>2</sup> is pyridinyl.

164. A compound or salt thereof according to claim 163, wherein the compound is selected from the group consisting of:

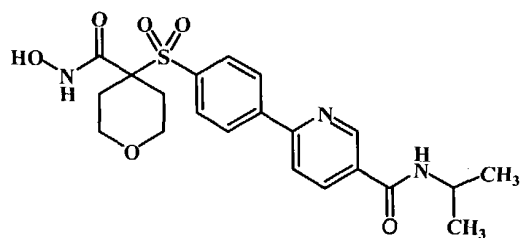




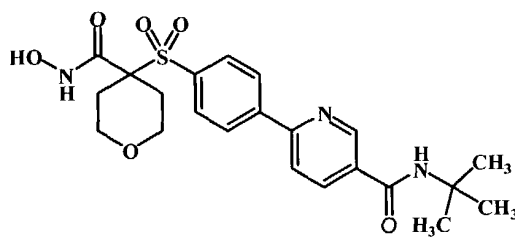
(164-3).

165. A compound or salt thereof according to claim 163, wherein E<sup>3</sup> is -C(O)-N(H)-.

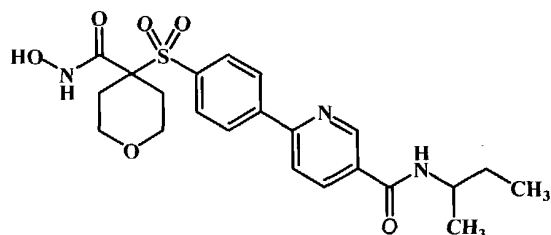
5 166. A compound or salt thereof according to claim 165, wherein the compound is selected from the group consisting of:



(166-1),



(166-2), and

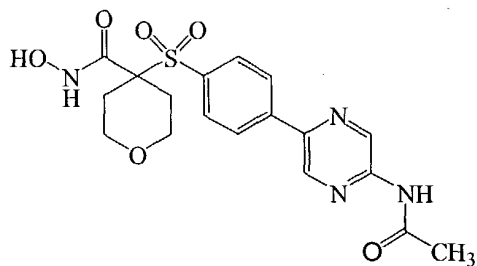


(166-3).

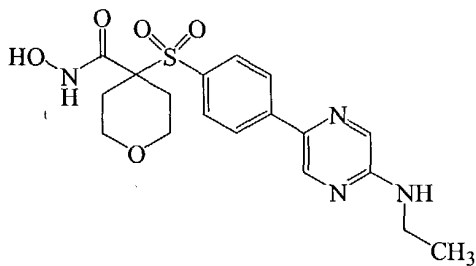
167. A compound or salt thereof according to claim 162, wherein E<sup>2</sup> is pyrazinyl.

10

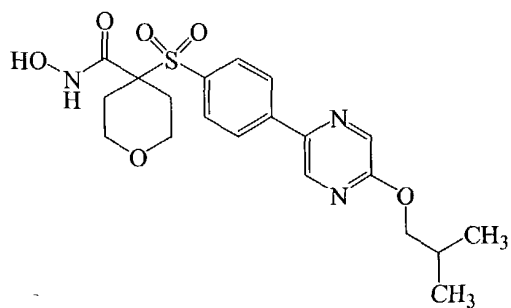
168. A compound or salt thereof according to claim 167, wherein the compound is selected from the group consisting of:



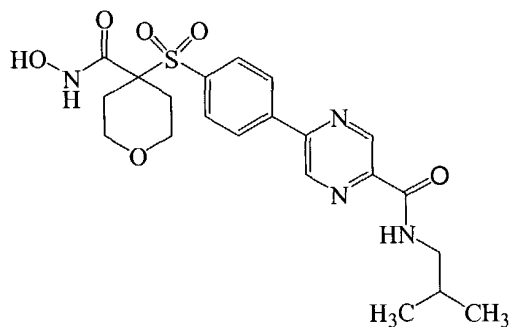
(168-1),



(168-2),



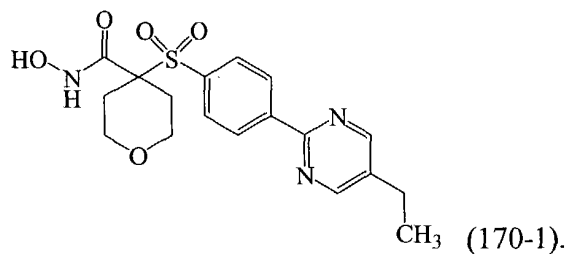
(168-3), and



(168-4).

169. A compound or salt thereof according to claim 162, wherein E<sup>2</sup> is pyrimidinyl.

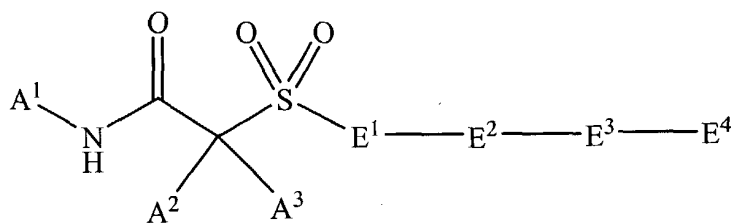
5 170. A compound or salt thereof according to claim 169, wherein the compound corresponds in structure to Formula (170-1):



(170-1).

171. A compound or a salt thereof, wherein:

10 the compound corresponds in structure to Formula (171-1):



(171-1); and

A<sup>1</sup> is selected from the group consisting of hydrogen, hydroxy, carbocycloxy, and heterocycloxy; and

as to A<sup>2</sup> and A<sup>3</sup>:

A<sup>2</sup> and A<sup>3</sup>, together with the carbon to which they are bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn,

optionally substituted with up to 3 independently selected R<sup>x</sup> substituents, or

A<sup>2</sup> and A<sup>3</sup> are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocycloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the heterocyclyl and carbocyclyl optionally are

substituted with up to 3 independently selected R<sup>x</sup> substituents; and

E<sup>1</sup> is aryl optionally substituted with one or more independently selected R<sup>x</sup> substituents; and

E<sup>2</sup> is heteroaryl, wherein the heteroaryl:

comprises at least two heteroatoms, and

is optionally substituted with one or more independently selected R<sup>x</sup> substituents; and

5 E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, -N(R<sup>b</sup>)-, -C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-, -C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-, alkyl, alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

10 any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R<sup>c</sup> substituents; and

E<sup>4</sup> is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, 15 carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein:

any such group optionally is substituted with one or more independently selected R<sup>d</sup> substituents; and

each R<sup>x</sup> is independently selected from the group consisting of halogen, cyano, 20 hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R<sup>b</sup>-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy, R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, 25 alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, 30 heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl,

heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and  $-R^{x1}-R^{x2}$ , wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently selected alkyl; and

each  $R^{x1}$  is independently selected from the group consisting of  $-C(O)-$ ,  $-C(S)-$ ,  $-C(NR^y)-$ , and  $-S(O)_2-$ ; and

each  $R^y$  is independently selected from the group consisting of hydrogen and hydroxy; and

each  $R^{x2}$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy,  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, and heterocyclyloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each  $R^b$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl,

carbocyclylalkyl, carbocyclyloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl,  
carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl,  
carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyloxyalkyl,  
heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl,  
5 heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl,  
aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl,  
10 alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R<sup>c</sup> is independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo,  
thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino,  
di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and

15 heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

20 each R<sup>d</sup> is independently selected from the group consisting of halogen,  
hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl,  
-N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>e</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocyclyl, alkylcarbocyclyl,  
carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more  
25 substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl,  
carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

30 any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino; and

each  $R^g$  is independently selected from the group consisting of hydrogen, alkyl,  
-O- $R^h$ , -N( $R^h$ )( $R^h$ ), carbocyclalkyl, and heterocyclalkyl, wherein:

5           any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino; and  
each  $R^h$  is independently selected from the group consisting of hydrogen, alkyl,  
10 carbocycl, carbocyclalkyl, heterocycl, and heterocyclalkyl, wherein:

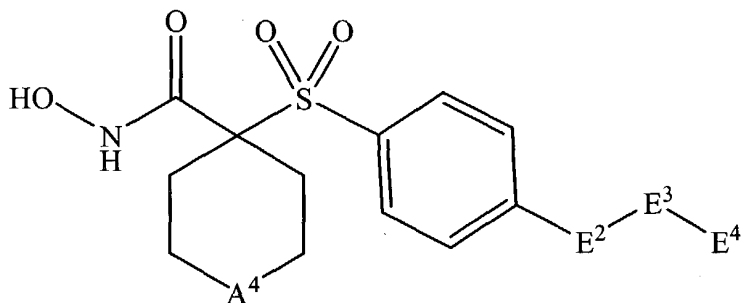
any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino,  
aminocarbonyl, and amino.

15

172. A compound or salt thereof according to claim 171, wherein  $E^1$  is  
phenyl.

173. A compound or salt thereof according to claim 172, wherein  $A^1$  is  
20 hydroxy.

174. A compound or salt thereof according to claim 173, wherein:  
the compound corresponds in structure to Formula (174-1):



(174-1); and

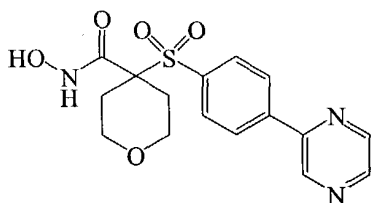
25            $A^4$  is selected from the group consisting of -O-, -N(H)-, -N( $R^x$ )-, -S-, -S(O)-,  
-S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C( $R^x$ )<sub>2</sub>-.

175. A compound or salt thereof according to claim 174, wherein  $-E^3-E^4$  is hydrogen.

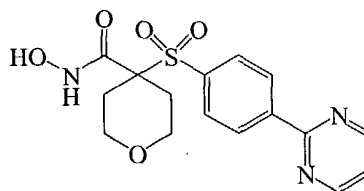
176. A compound or salt thereof according to claim 175, wherein  $E^2$  is  
5 single-ring heteroaryl.

177. A compound or salt thereof according to claim 176, wherein  $E^2$  is selected from the group consisting of pyrimidinyl and pyrazinyl.

10 178. A compound or salt thereof according to claim 177, wherein the compound is selected from the group consisting of:



(178-1), and



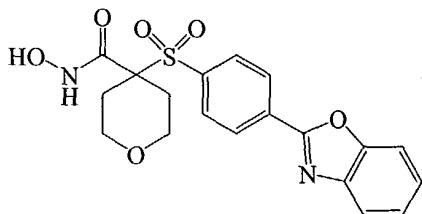
(178-2).

179. A compound or salt thereof according to claim 174, wherein  $E^2$  is a fused-ring heteroaryl.

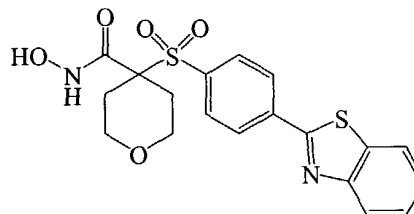
15

180. A compound or salt thereof according to claim 179, wherein  $E^2$  is a 9-member heteroaryl.

181. A compound or salt thereof according to claim 180, wherein the  
20 compound is selected from the group consisting of:



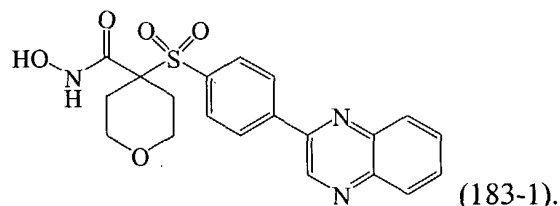
(181-1), and



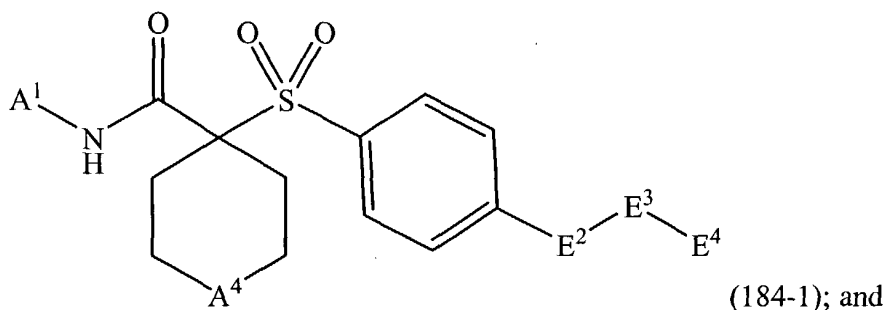
(181-2).

182. A compound or salt thereof according to claim 179, wherein E<sup>2</sup> is a 10-member heteroaryl.

183. A compound or salt thereof according to claim 182, wherein the  
5 compound corresponds in structure to Formula (183-1):



184. A compound or a salt thereof, wherein:  
the compound corresponds in structure to Formula (184-1):



A<sup>1</sup> is selected from the group consisting of hydrogen, hydroxy, carbocycloxy, and heterocycloxy; and

A<sup>4</sup> is selected from the group consisting of -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-; and

E<sup>2</sup> is selected from the group consisting of aryl and heteroaryl, wherein:

the aryl or heteroaryl optionally substituted with one or more independently selected R<sup>x</sup> substituents; and

E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, -N(R<sup>b</sup>)-, -C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-, -C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-, alkyl, alkenyl, carbonylalkyl, and alkylcarbonyl, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected  $R^c$  substituents; and

$E^4$  is selected from the group consisting of alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein:

any such group optionally is substituted with one or more independently selected  $R^d$  substituents; and

each  $R^x$  is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy, alkylthio,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and  $-R^{x1}-R^{x2}$ , wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently selected alkyl; and

each  $R^{x1}$  is independently selected from the group consisting of  $-C(O)-$ ,  $-C(S)-$ ,  $-C(NR^y)-$ , and  $-S(O)_2-$ ; and

5 each  $R^y$  is independently selected from the group consisting of hydrogen and hydroxy; and

each  $R^{x2}$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy,  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocycliloxy, carbocycliloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocycliloxy, and heterocycliloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

20 each  $R^b$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocycliloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocycliloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R<sup>d</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, -N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>g</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl, -O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclylalkyl, and heterocyclylalkyl, wherein:

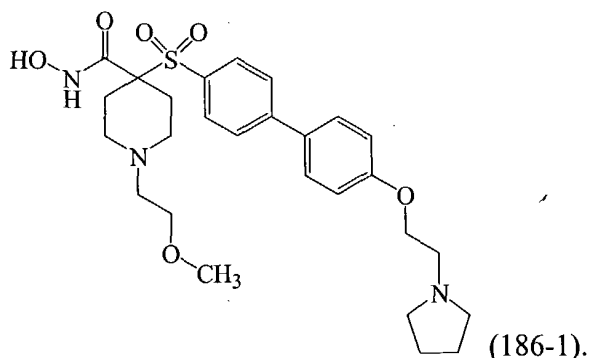
any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each  $R^h$  is independently selected from the group consisting of hydrogen, alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

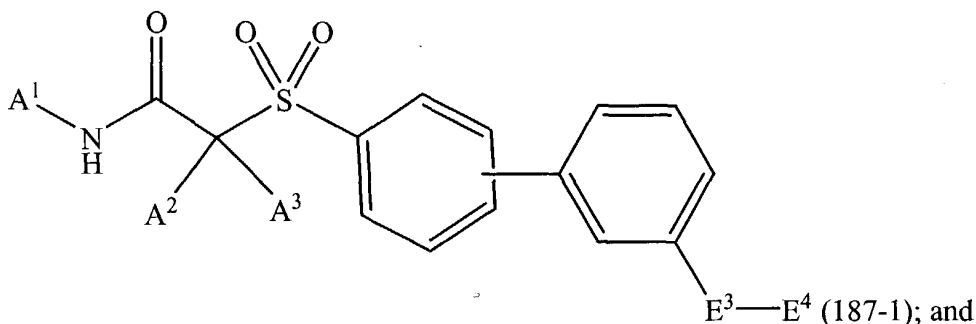
any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

185. A compound or salt thereof according to claim 184, wherein  $A^1$  is hydroxy.

186. A compound or salt thereof according to claim 185, wherein the compound corresponds in structure to Formula (186-1):



187. A compound or a salt thereof, wherein:  
the compound corresponds in structure to Formula (187-1):



$A^1$  is selected from the group consisting of hydrogen, hydroxy, carbocycloxy, and heterocycloxy; and

as to  $A^2$  and  $A^3$ :

A<sup>2</sup> and A<sup>3</sup>, together with the carbon to which they are bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R<sup>x</sup> substituents, or

A<sup>2</sup> and A<sup>3</sup> are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyoxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyoxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the heterocyclyl and carbocyclyl optionally are

substituted with up to 3 independently selected R<sup>x</sup> substituents; and

E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, -N(R<sup>b</sup>)-, -C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-, -C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-, alkyl, alkenyl, carbonylalkyl, and alkylcarbonyl, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R<sup>c</sup> substituents; and

E<sup>4</sup> is selected from the group consisting of alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein:

any such group optionally is substituted with one or more independently selected R<sup>d</sup> substituents; and

each R<sup>x</sup> is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R<sup>b</sup>-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy, R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocycliloxy, carbocycliloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocycliloxy, heterocycliloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and -R<sup>x1</sup>-R<sup>x2</sup>, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thiooxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently  
selected alkyl; and

each  $R^{x1}$  is independently selected from the group consisting of -C(O)-, -C(S)-,  
-C(NR<sup>y</sup>)-, and -S(O)<sub>2</sub>-; and

5 each R<sup>y</sup> is independently selected from the group consisting of hydrogen and  
hydroxy; and

each  $R^{x2}$  is independently selected from the group consisting of hydrogen,  
hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R<sup>b</sup>-oxyalkyl,  
alkenyloxy, alkynyloxy, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy,

10 R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocyclyoxy,  
carbocyclyoxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocyclyoxy, and  
heterocyclyoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
15 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl,  
alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are  
substituted with one or more substituents independently selected from  
the group consisting of halogen and hydroxy; and

20 each R<sup>b</sup> is independently selected from the group consisting of hydrogen,  
hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl,  
alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl,  
carbocyclylalkyl, carbocyclyoxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl,  
carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl,  
25 carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocyclyoxyalkyl,  
heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl,  
heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl,  
aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more  
30 substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R<sup>d</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, -N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>e</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl, -O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclylalkyl, and heterocyclylalkyl, wherein:

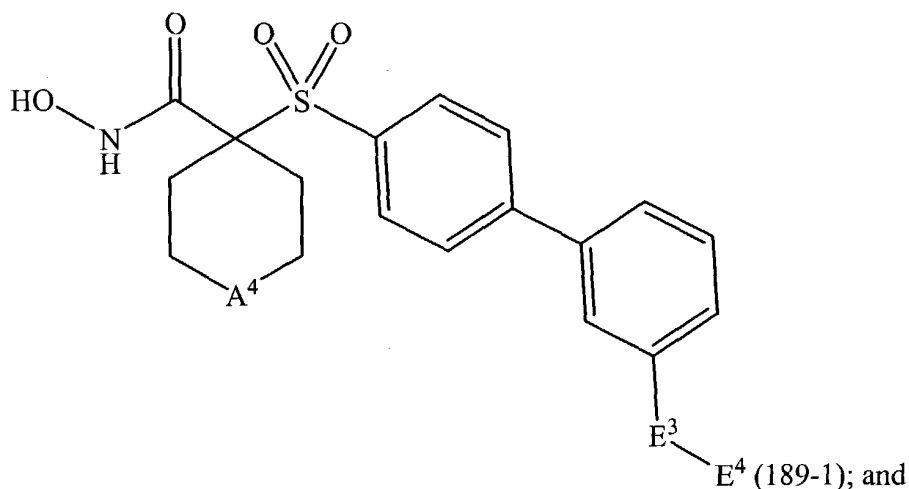
any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>h</sup> is independently selected from the group consisting of hydrogen, alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

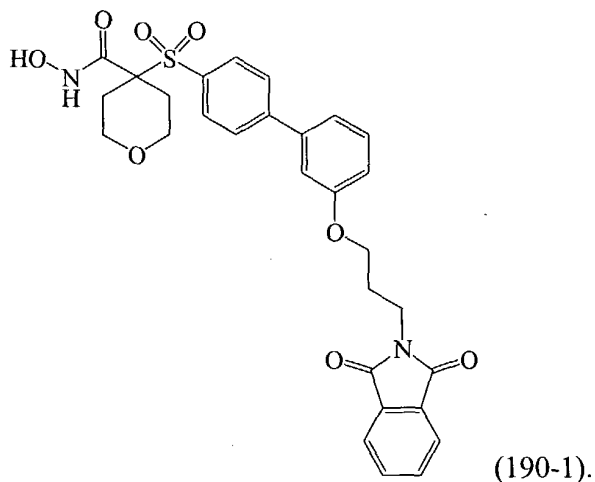
188. A compound or salt thereof according to claim 187, wherein A<sup>1</sup> is hydroxy.

189. A compound or salt thereof according to claim 188, wherein: the compound corresponds in structure to Formula (189-1):

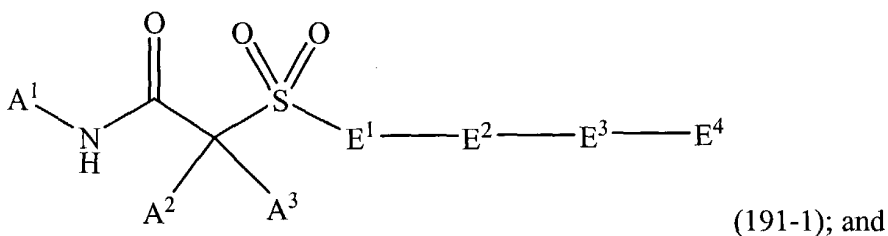


A<sup>4</sup> is selected from the group consisting of -O-, -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-.

190. A compound or salt thereof according to claim 189, wherein the compound corresponds in structure to Formula (190-1):



191. A compound or a salt thereof, wherein:  
the compound corresponds in structure to Formula (191-1):



A<sup>1</sup> is selected from the group consisting of hydrogen, hydroxy, carbocycloxy, and heterocycloxy; and

as to A<sup>2</sup> and A<sup>3</sup>:

A<sup>2</sup> and A<sup>3</sup>, together with the carbon to which they are bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn, optionally substituted with up to 3 independently selected R<sup>x</sup> substituents, or

A<sup>2</sup> and A<sup>3</sup> are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyoxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyoxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the heterocyclyl and carbocyclyl optionally are

substituted with up to 3 independently selected R<sup>x</sup> substituents; and

E<sup>1</sup> is aryl optionally substituted with one or more independently selected R<sup>x</sup> substituents; and

E<sup>2</sup> is 2 rings fused together, wherein:

the ring bonded to E<sup>1</sup> is an unsaturated, 6-member ring, one or both of the rings comprise one or more independently selected heteroatoms, and

one or both of the rings optionally are substituted with one or more independently selected R<sup>x</sup> substituents; and

E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, -N(R<sup>b</sup>)-, -C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-, -C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-, alkyl, alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R<sup>c</sup> substituents; and

E<sup>4</sup> is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl,

5 wherein:

any such group optionally is substituted with one or more independently selected R<sup>d</sup> substituents; and

each R<sup>x</sup> is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,

10 R<sup>b</sup>-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy, R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, 15 alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, 20 heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and -R<sup>x1</sup>-R<sup>x2</sup>, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thiooxo, imino, 25 alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently selected alkyl; and 30

each  $R^{X1}$  is independently selected from the group consisting of -C(O)-, -C(S)-, -C(NR<sup>y</sup>)-, and -S(O)<sub>2</sub>-; and

each R<sup>y</sup> is independently selected from the group consisting of hydrogen and hydroxy; and

5 each  $R^{X2}$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R<sup>b</sup>-oxyalkyl, alkenyloxy, alkynyloxy, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy, R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocycloxy, carbocycloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocycloxy, and  
10 heterocycloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

15 the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R<sup>b</sup> is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocycloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and  
30

each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and

5 heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

10 each R<sup>d</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, -N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>g</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

15 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

20 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

25 each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl, -O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclylalkyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

30 each R<sup>h</sup> is independently selected from the group consisting of hydrogen, alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

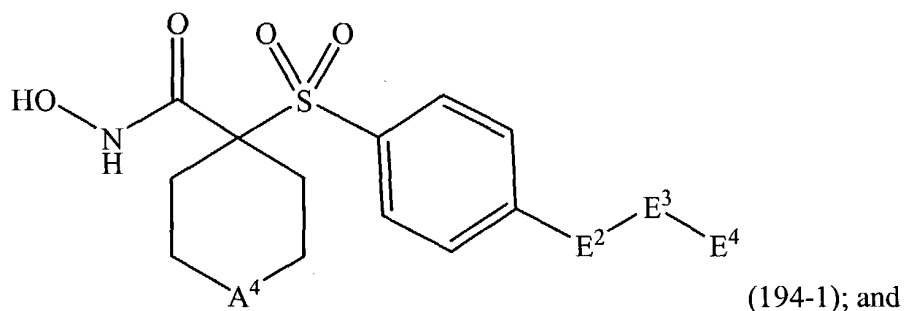
any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

5

192. A compound or salt thereof according to claim 191, wherein E<sup>1</sup> is phenyl.

193. A compound or salt thereof according to claim 192, wherein A<sup>1</sup> is  
10 hydroxy.

194. A compound or salt thereof according to claim 193, wherein:  
the compound corresponds in structure to Formula (194-1):



15 A<sup>4</sup> is selected from the group consisting of -O-, -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-.

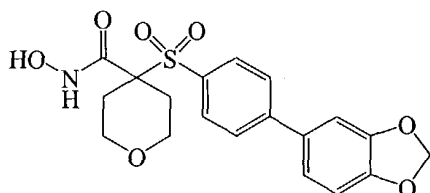
195. A compound or salt thereof according to claim 194, wherein E<sup>2</sup> is 10-member heterocyclyl.

20

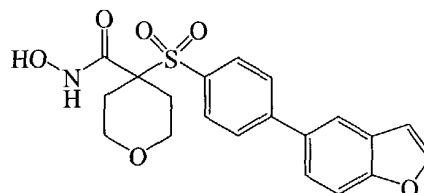
196. A compound or salt thereof according to claim 194, wherein E<sup>2</sup> is 9-member heterocyclyl.

197. A compound or salt thereof according to claim 196, wherein -E<sup>3</sup>-E<sup>4</sup> is  
25 hydrogen.

198. A compound or salt thereof according to claim 197, wherein the compound is selected from the group consisting of:



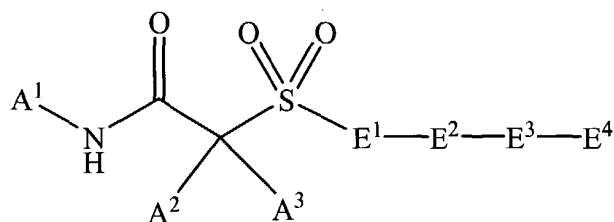
(198-1), and



(198-2).

199. A compound or a salt thereof, wherein:

5 the compound corresponds in structure to Formula (199-1):



(199-1); and

A<sup>1</sup> is selected from the group consisting of hydrogen, hydroxy, carbocycloxy, and heterocycloxy; and

as to A<sup>2</sup> and A<sup>3</sup>:

10 A<sup>2</sup> and A<sup>3</sup>, together with the carbon to which they are bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

15 the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn,

optionally substituted with up to 3 independently selected R<sup>x</sup> substituents, or

20 A<sup>2</sup> and A<sup>3</sup> are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocycloxyalkyl,

carbocyclalkoxyalkyl, carbocyclalkylthio, carbocyclthioalkyl,  
carbocyclalkylthioalkyl, heterocycl, heterocyclalkyl, heterocyclalkenyl,  
heterocyclalkynyl, heterocycloxyalkyl, heterocyclalkoxyalkyl,  
heterocyclalkylthio, heterocyclthioalkyl, and heterocyclalkylthioalkyl,

wherein:

any member of such group optionally is substituted with up to 3  
independently selected R<sup>x</sup> substituents, and

any member of such group optionally is substituted with two  
substituents such that the two substituents, together with the atom(s) to  
which they are bonded, form a carbocycl or heterocycl, wherein:

the heterocycl and carbocycl optionally are

substituted with up to 3 independently selected R<sup>x</sup> substituents;  
and

E<sup>1</sup> is aryl optionally substituted with one or more independently selected R<sup>x</sup>

substituents; and

E<sup>2</sup> is selected from the group consisting of aryl and heteroaryl, wherein:

the aryl or heteroaryl optionally substituted with one or more  
independently selected R<sup>x</sup> substituents; and

-E<sup>3</sup>-E<sup>4</sup> is selected from the group consisting of -CH<sub>2</sub>-CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>2</sub>-CH<sub>3</sub>,

-C(CH<sub>3</sub>)<sub>2</sub>H, and -O-CH<sub>2</sub>-CH<sub>3</sub>, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkoxy, alkoxyalkyl,  
-N(R<sup>c</sup>)(R<sup>c</sup>), -C(O)(R<sup>b</sup>), -S-R<sup>c</sup>, -S(O)<sub>2</sub>-R<sup>c</sup>, carbocycl, alkylcarbocycl,  
carbocyclalkyl, heterocycl, alkylheterocycl, and heterocyclalkyl,  
wherein:

any member of such group optionally is substituted with one or  
more substituents independently selected from the group consisting of  
halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo,  
thioxo, imino, aminocarbonyl, and amino; and

each  $R^X$  is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy,  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy, alkylthio,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,  $R^bR^b$ -aminoalkyl( $R^b$ )amino, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxy, carbocyclylalkoxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclylalkoxy, heterocyclylalkoxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and  $-R^{x1}-R^{x2}$ , wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and the amino optionally is substituted with up to 2 independently selected alkyl; and

each  $R^{x1}$  is independently selected from the group consisting of  $-C(O)-$ ,  $-C(S)-$ ,  $-C(NR^y)-$ , and  $-S(O)_2-$ ; and

each  $R^y$  is independently selected from the group consisting of hydrogen and hydroxy; and

each  $R^{x2}$  is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy,  $R^b$ -oxyalkyl, alkenyloxy, alkynyloxy,  $R^bR^b$ -amino,  $R^bR^b$ -aminoalkyl,  $R^bR^b$ -aminoalkoxy,

R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocycloxy, carbocycloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocycloxy, and heterocycloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy; and

each R<sup>b</sup> is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocycloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl, carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocycloxyalkyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclalkyl; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl, carbocycl, carbocyclalkyl, heterocycl, and heterocyclalkyl, wherein:

5           any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl, 10 -O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclalkyl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

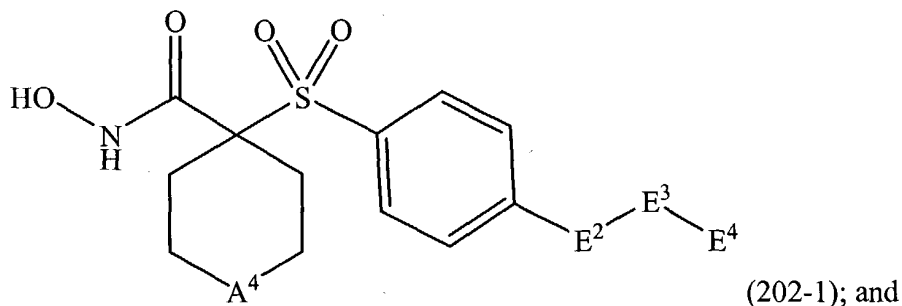
15           each R<sup>h</sup> is independently selected from the group consisting of hydrogen, alkyl, carbocycl, carbocyclalkyl, heterocycl, and heterocyclalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, 20 aminocarbonyl, and amino.

200. A compound or salt thereof according to claim 199, wherein E<sup>1</sup> is phenyl.

25           201. A compound or salt thereof according to claim 200, wherein A<sup>1</sup> is hydroxy.

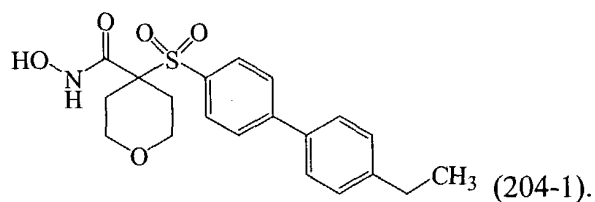
202. A compound or salt thereof according to claim 201, wherein:  
the compound corresponds in structure to Formula (202-1):



A<sup>4</sup> is selected from the group consisting of -O-, -N(H)-, -N(R<sup>x</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -C(H)<sub>2</sub>-, and -C(R<sup>x</sup>)<sub>2</sub>-.

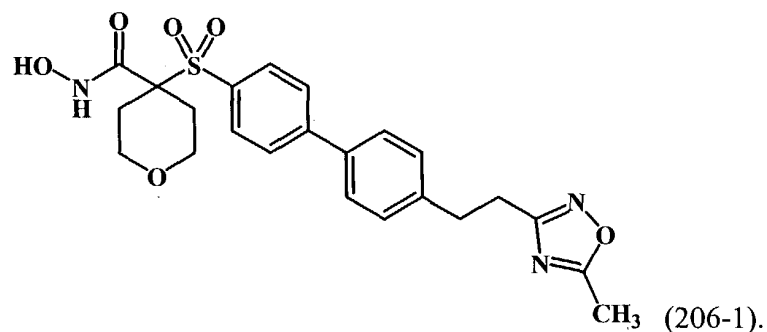
203. A compound or salt thereof according to claim 202, wherein -E<sup>3</sup>-E<sup>4</sup> is -CH<sub>2</sub>-CH<sub>3</sub>.

204. A compound or salt thereof according to claim 203, wherein the compound corresponds in structure to Formula (204-1):



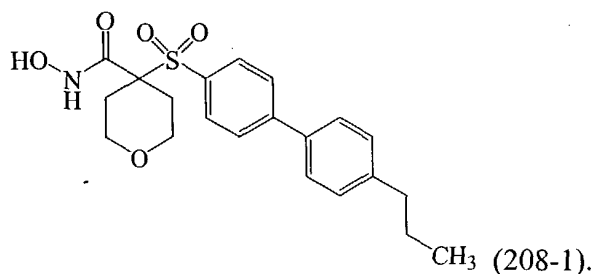
205. A compound or salt thereof according to claim 202, wherein -E<sup>3</sup>-E<sup>4</sup> is -CH<sub>2</sub>-CH<sub>3</sub> substituted with alkylheterocyclyl

206. A compound or salt thereof according to claim 205, wherein the compound corresponds in structure to Formula (206-1):



207. A compound or salt thereof according to claim 202, wherein  $-E^3-E^4$  is  $-(CH_2)_2-CH_3$ .

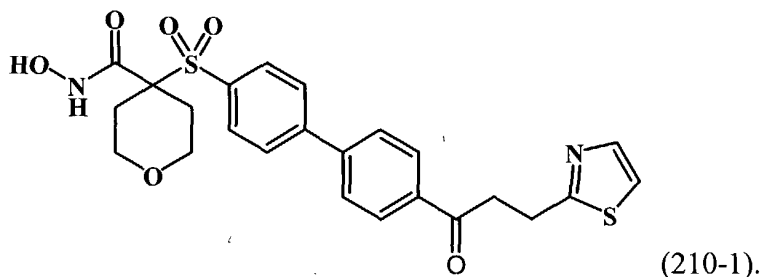
208. A compound or salt thereof according to claim 207, wherein the  
5 compound corresponds in structure to Formula (208-1):



209. A compound or salt thereof according to claim 202, wherein  $-E^3-E^4$  is  $-(CH_2)_2-CH_3$  substituted with heterocyclyl and oxo.

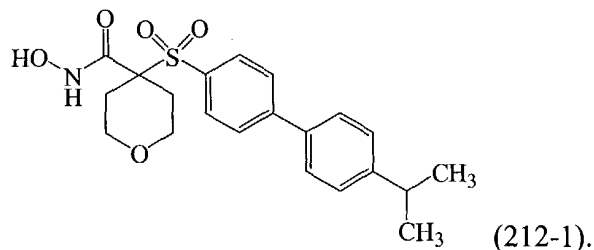
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210. A compound or salt thereof according to claim 209, wherein the  
compound corresponds in structure to Formula (210-1):



211. A compound or salt thereof according to claim 202, wherein  $-E^3-E^4$  is  $-C(CH_3)_2H$ .

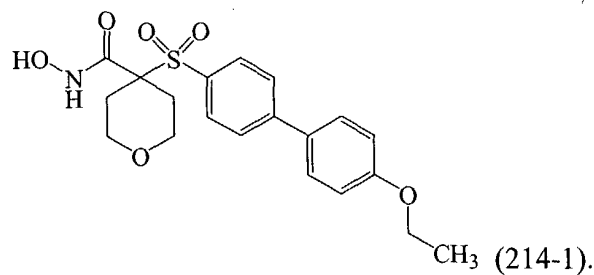
212. A compound or salt thereof according to claim 211, wherein the  
compound corresponds in structure to Formula (212-1):



213. A compound or salt thereof according to claim 202, wherein -E<sup>3</sup>-E<sup>4</sup> is -O-CH<sub>2</sub>-CH<sub>3</sub>.

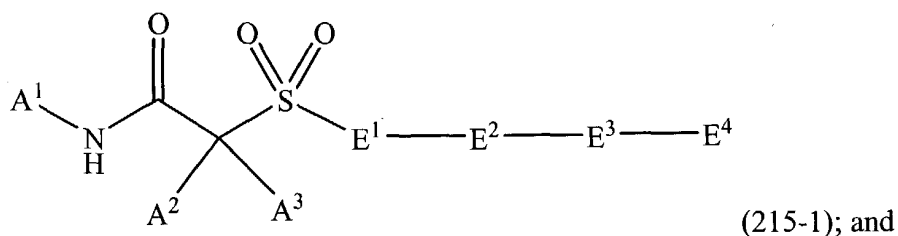
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214. A compound or salt thereof according to claim 213, wherein the compound corresponds in structure to Formula (214-1):



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215. A compound or a salt thereof, wherein:  
the compound corresponds in structure to Formula (215-1):



A<sup>1</sup> is selected from the group consisting of hydrogen, hydroxy, carbocycloxy, and heterocycloxy; and

15

as to A<sup>2</sup> and A<sup>3</sup>:

A<sup>2</sup> and A<sup>3</sup>, together with the carbon to which they are bonded, form heterocyclyl or carbocyclyl, wherein:

the heterocyclyl or carbocyclyl optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

the heterocyclyl or carbocyclyl optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

the optional heterocyclyl or carbocyclyl is, in turn,

5 optionally substituted with up to 3 independently selected R<sup>x</sup> substituents, or

A<sup>2</sup> and A<sup>3</sup> are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyoxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyoxyalkyl, heterocyclylalkoxyalkyl, heterocyclylalkylthio, heterocyclylthioalkyl, and heterocyclylalkylthioalkyl, wherein:

15 any member of such group optionally is substituted with up to 3 independently selected R<sup>x</sup> substituents, and

any member of such group optionally is substituted with two substituents such that the two substituents, together with the atom(s) to which they are bonded, form a carbocyclyl or heterocyclyl, wherein:

20 the heterocyclyl and carbocyclyl optionally are substituted with up to 3 independently selected R<sup>x</sup> substituents; and

E<sup>1</sup> is aryl optionally substituted with one or more independently selected R<sup>x</sup> substituents; and

25 E<sup>2</sup> is naphthyl optionally substituted with one or more independently selected R<sup>x</sup> substituents; and

E<sup>3</sup> is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-, -N(R<sup>b</sup>)-, -C(O)-N(R<sup>b</sup>)-, -N(R<sup>b</sup>)-C(O)-, -C(O)-N(R<sup>b</sup>)-N(R<sup>b</sup>)-C(O)-, -N(R<sup>b</sup>)-C(O)-N(R<sup>b</sup>)-, -S-, -S(O)-, -S(O)<sub>2</sub>-, -N(R<sup>b</sup>)-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-N(R<sup>b</sup>)-, -O-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-O-, -C(NH)-, -C(NOH)-, -N(R<sup>b</sup>)-C(NH)-, -N(R<sup>b</sup>)-C(NOH)-, -C(NH)-N(R<sup>b</sup>)-, -C(NOH)-N(R<sup>b</sup>)-, alkyl, alkenyl, carbonylalkyl, alkylcarbonyl, and a bond, wherein:

any alkyl or alkenyl portion of a substituent in such group optionally is substituted with one or more independently selected R<sup>c</sup> substituents; and

E<sup>4</sup> is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkoxyalkyl, heterocyclyl, heterocyclylalkyl, and heterocyclylalkoxyalkyl, wherein:

any such group optionally is substituted with one or more independently selected R<sup>d</sup> substituents; and

each R<sup>x</sup> is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkoxy, R<sup>b</sup>-oxyalkyl, alkenyloxy, alkynyloxy, alkylthio, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy, R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocyclyloxy, carbocyclyloxyalkoxy, carbocyclylthio, heterocyclyl, heterocyclylalkyl, heterocyclyloxy, heterocyclyloxyalkoxy, heterocyclylthio, alkyliminocarbonyl, alkylthioalkyl, alkylsulfonylalkyl, alkylsulfoxidoalkyl, alkylthioalkenyl, alkylsulfoxidoalkenyl, alkylsulfonylalkenyl, carbocyclylalkoxyalkyl, carbocyclyliminocarbonyl, carbocyclylthioalkyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonylalkyl, carbocyclylthioalkenyl, carbocyclylsulfoxidoalkenyl, carbocyclylsulfonylalkenyl, heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl, heterocyclylsulfonylalkyl, heterocyclylthioalkenyl, heterocyclylsulfoxidoalkenyl, heterocyclylsulfonylalkenyl, heterocyclyliminocarbonyl, aminosulfonylalkyl, and -R<sup>x1</sup>-R<sup>x2</sup>, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently  
selected alkyl; and

each  $R^{x1}$  is independently selected from the group consisting of -C(O)-, -C(S)-,  
-C(NR<sup>y</sup>)-, and -S(O)<sub>2</sub>-; and

5 each R<sup>y</sup> is independently selected from the group consisting of hydrogen and  
hydroxy; and

each  $R^{x2}$  is independently selected from the group consisting of hydrogen,  
hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R<sup>b</sup>-oxyalkyl,  
alkenyloxy, alkynyloxy, R<sup>b</sup>R<sup>b</sup>-amino, R<sup>b</sup>R<sup>b</sup>-aminoalkyl, R<sup>b</sup>R<sup>b</sup>-aminoalkoxy,

10 R<sup>b</sup>R<sup>b</sup>-aminoalkyl(R<sup>b</sup>)amino, carbocyclyl, carbocyclylalkyl, carbocycliloxy,  
carbocycliloxyalkoxy, heterocyclyl, heterocyclylalkyl, heterocycliloxy, and  
heterocycliloxyalkoxy, wherein:

any member of such group optionally is substituted with one or more  
substituents independently selected from the group consisting of halogen,  
15 hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl,  
alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

the alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy optionally are  
substituted with one or more substituents independently selected from  
the group consisting of halogen and hydroxy; and

20 each R<sup>b</sup> is independently selected from the group consisting of hydrogen,  
hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl,  
alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl,  
carbocyclylalkyl, carbocycliloxyalkyl, carbocyclylalkoxyalkyl, carbocyclylthioalkyl,  
carbocyclylthioalkenyl, carbocyclylsulfoxidoalkyl, carbocyclylsulfonyl,  
25 carbocyclylsulfonylalkyl, heterocyclyl, heterocyclylalkyl, heterocycliloxyalkyl,  
heterocyclylalkoxyalkyl, heterocyclylthioalkyl, heterocyclylsulfoxidoalkyl,  
heterocyclylsulfonyl, heterocyclylsulfonylalkyl, aminoalkyl, aminosulfonyl,  
aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein:

any member of such group optionally is substituted with one or more  
30 substituents independently selected from the group consisting of halogen,

hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl; and

each R<sup>c</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, -C(H)(NH), -C(H)(NOH), thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino, alkyl, alkoxy, alkenyl, alkynyl, alkoxyalkyl, mono-alkylamino, di-alkylamino, alkylthio, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, amino, alkyl, and carbocyclylalkyl; and

each R<sup>d</sup> is independently selected from the group consisting of halogen, hydroxy, cyano, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, -N(R<sup>e</sup>)(R<sup>e</sup>), -C(O)(R<sup>e</sup>), -S-R<sup>e</sup>, -S(O)<sub>2</sub>-R<sup>e</sup>, carbocyclyl, alkylcarbocyclyl, carbocyclylalkyl, heterocyclyl, alkylheterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>e</sup> is independently selected from the group consisting of hydrogen alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R<sup>g</sup> is independently selected from the group consisting of hydrogen, alkyl, -O-R<sup>h</sup>, -N(R<sup>h</sup>)(R<sup>h</sup>), carbocyclylalkyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

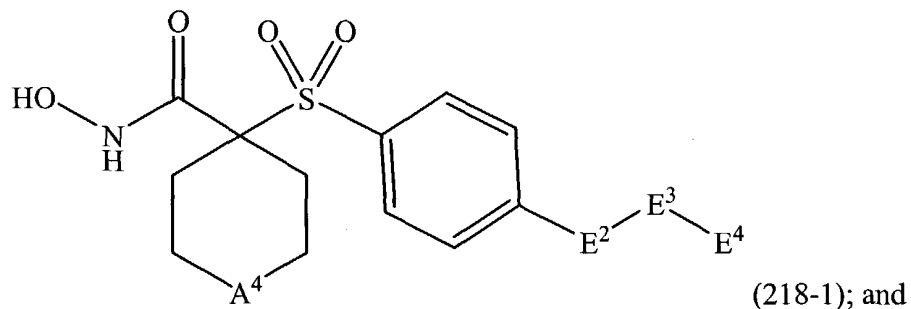
each  $R^h$  is independently selected from the group consisting of hydrogen, alkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

216. A compound or salt thereof according to claim 215, wherein  $E^1$  is phenyl.

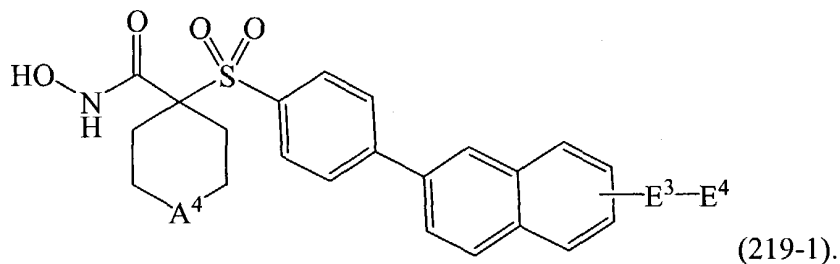
217. A compound or salt thereof according to claim 215, wherein  $A^1$  is hydroxy.

218. A compound or salt thereof according to claim 217, wherein:  
the compound corresponds in structure to Formula (218-1):

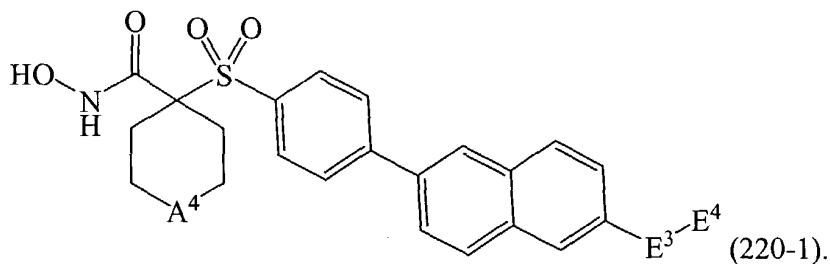


$A^4$  is selected from the group consisting of  $-O-$ ,  $-N(H)-$ ,  $-N(R^x)-$ ,  $-S-$ ,  $-S(O)-$ ,  $-S(O)_2-$ ,  $-C(H)_2-$ , and  $-C(R^x)_2-$ .

219. A compound or salt thereof according to claim 218, wherein the compound corresponds in structure to Formula (219-1):



220. A compound or salt thereof according to claim 219, wherein the compound corresponds in structure to Formula (220-1):

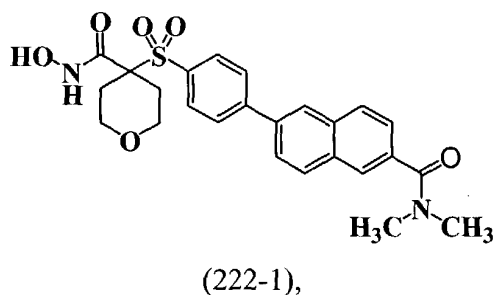


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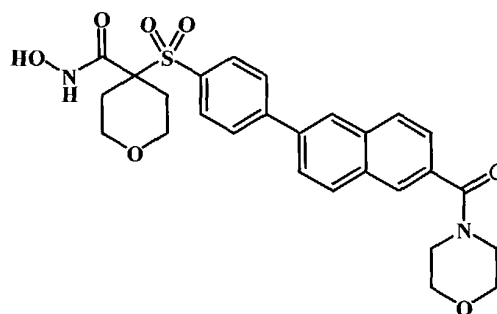
221. A compound or salt thereof according to claim 220, wherein  $E^3$  is selected from the group consisting of  $-C(O)-$  and  $-C(O)-N(R^b)-$ .

222. A compound or salt thereof according to claim 221, wherein the compound is selected from the group consisting of:

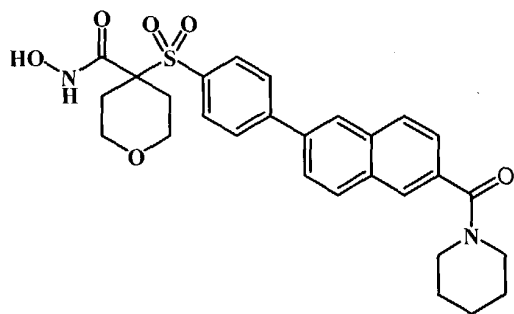
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(222-1),



(222-2), and



(222-3).

223. A method for treating a condition associated with pathologically excessive matrix metalloprotease activity, TNF- $\alpha$  convertase activity, or aggrecanase

activity in a mammal, wherein the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1, 75, 80, 94, 135, 157, 171, 184, 187, 191, 199, and 215 to the mammal in an amount that is therapeutically-effective to treat the condition.

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224. A method according to claim 223, wherein A<sup>1</sup> is selected from the group consisting of hydrogen and hydroxy.

225. A method for treating a pathological condition in a mammal, wherein:

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the pathological condition is selected from the group consisting of tissue destruction, a fibrotic disease, matrix weakening, defective injury repair, a cardiovascular disease, a pulmonary disease, a kidney disease, a liver disease, an ophthalmologic disease, and a central nervous system disease; and

the method comprises administering a compound (or a pharmaceutically acceptable salt thereof) recited in claim 1, 75, 80, 94, 135, 157, 171, 184, 187, 191, 199, and 215 to the mammal in an amount that is therapeutically-effective to treat the pathological condition.

15

226. A pharmaceutical composition, wherein the composition comprises a

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therapeutically-effective amount of a compound (or a pharmaceutically-acceptable salt thereof) recited in claim 1, 75, 80, 94, 135, 157, 171, 184, 187, 191, 199, and 215.